VOLUME VI • NUMBER 3 • AUGUST 1961

ANNALS OF PHYSICAL MEDICINE

The Official Organ of the British Association of Physical Medicine

London
BAILLIÈRE, TINDALL AND COX
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ANNALS OF PHYSICAL MEDICINE

The Official Organ of the
BRITISH ASSOCIATION OF PHYSICAL MEDICINE

Vol. VI August 1961 No. 3

ORIGINAL PAPER

CHONDROLYSIS*

By CHARLES H. LACK

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CARTILAGE cells synthesize a matrix of chondromucin, which is a complex containing about 30% protein and 70% chondroitin sulphate (Shatton and Schubert, 1954; Gross, Mathews, and Dorfman, 1960). It appears that the chondroitin-sulphate–protein complex is extruded from the chondrocyte as a unit. Collagen or elastic fibres form a meshwork within this matrix and may form molecular associations with the mucopolysaccharide. A discussion on the breakdown of cartilage must at present be restricted to the dissolution of the matrix, as we are ignorant of physiological collagenases.

Chondrolysis may result from enzymatic attack on the matrix from without, or from release of enzymes from the chondrocytes, or from interference with their proper synthesis of chondromucin. Known factors operating at these different levels are set out in Table I overleaf.

The action of excess vitamin A (Thomas *et al.*, 1960; Fell and Thomas, 1960) appears to result in the release of mucolytic enzyme from the chondrocytes. Lathyrism caused by the ingestion of sweet-pea seeds is a mesenchymal disorder in which vascular, skeletal, and connective-tissue lesions develop. The nitriles and other lathyrogenic agents have been shown to inhibit the synthesis of sulphated mucopolysaccharides (Karnovsky and Karnovsky, 1961), and this accounts for the degenerative changes in cartilage. Cortisone and salicylate depress chondrogenesis by inhibiting the sulphation, not the biosynthesis, of chondroitin sulphate (Whitehouse and Lash, 1961).

* Paper read at the Annual Meeting of the British Association of Physical Medicine, London, April 21, 1961.

These studies on the cellular level are too recent to warrant further comment, but obviously they hold great promise for a better understanding of the metabolism not only of cartilage but of all mesenchymal tissues.

Turning to the commoner conditions under which we observe dissolution of cartilage, pyogenic infection is undoubtedly the most destructive. Phemister (1924) studied the digestion of articular cartilage in staphylococcal pus and attributed this to enzyme released from polymorphonulear leucocytes. Tuberculous pus was not chrondrolytic, and this was attributed to its predominance of lymphocytes. Ziff, Gribetz, and Lospalluto (1960) have recently shown that extracts of polymorphonuclear leucocytes degrade chondromucin; lymphocytes were not only inactive

TABLE I

THE ACTION OF CHONDROLYTIC AGENTS ON DIFFERENT COMPONENTS OF CARTILAGE

	CELLS	MATRIX (Chondromucin)	FIBRES
COMPONENT	Chrondrocytes	Chondroitin-sulphate –protein complex	Collagen Elastin
AGENT	(1) Vitamin A (2) Nitriles (lathyrism) (3) Cortisone ?Salicylate	Leucoprotease Plasmin Papain	
ACTION	(1) Release of cellular protease (2) Inhibition of synthesis of matrix (3) Inhibition of sulphation of chondroitin	Proteolysis and release of chondroitin sulphate	

but, when added in excess to granulocytes, appeared to inhibit the activity of the latter. Ziff also showed that extracts of rheumatoid synovial membranes reduced the viscosity of chondromucin and that this activity was proportional to the amount of cellular infiltration.

When we attempt to relate the speed and extent of cartilage destruction in suppurative arthritis to the cell counts in the synovial fluid it becomes apparent that in some streptococcal and staphylococcal infections another factor is operating. Chondrolysis in some of these cases may be tragically quick and devastating, with subsequent bony ankylosis. Most pathogenic strains of these cocci produce activators of the blood proenzyme plasminogen, converting it to the protease plasmin; these activators are called streptokinase and staphylokinase respectively.

When pieces of cartilage are incubated with plasmin there is a release of

chrondroitin sulphate (Lack and Rogers, 1958), and when chondromucin is incubated with plasmin there is a reduction in viscosity comparable to that caused by leucocyte extract, but, unlike the latter, plasmin digestion is inhibited by soybean trypsin inhibitor. Plate III, Fig. 1 shows a slice of cartilage taken with a freezing microtome, incubated in plasminogen, then stained with toluidine blue; Plate III, Fig. 2 shows a similar slice incubated for the same time in the same concentration of plasminogen to which staphylokinase has been added. The staphylokinase has activated the plasminogen and the plasmin has caused a marked depletion of matrix.

Before discussing the chondrolytic activity of plasmin any further, we should perhaps first consider its physiological role, especially in the joint. Plasminogen is a blood protein and does not appear in synovial fluid unless there has been haemorrhage or an increased permeability of the blood-vessels, in which cases fibrinogen and plasminogen pass into the synovial fluid. If clotting occurs, plasminogen is incorporated in the clot. Both synovial membrane and cartilage contain activators

TABLE II

THE PLASMIN SYSTEM

Proenzyme	Activators	Protease	Inhibitors
Plasminogen	Damaged tissues and leucocytes	Plasmin	α^1-globulins α^2-globulins
		Substrates	
	Staphylokinase Streptokinase activator	Fibrin Chrondomucin ? Intercellular cement	Split products
	Urokinase, etc.		Soy bean

of plasminogen, so that clot forming on these tissues is rapidly dissolved. Plasmin coming away after fibrinolysis is quickly neutralized by inhibitor in the synovial fluid. This physiological clearing mechanism ensures the removal of clot from joint tissues without damage to anything else.

The principal factors involved in the plasmin system are set out in Table II, and it is obvious that when streptokinase or staphylokinase, as well as additional tissue activator from leucocytes, is superimposed on to the physiological mechanism, the local inhibitor may be unable to neutralize the excess of plasmin, which is then free to attack the cartilage matrix.

In staphylococcal or streptococcal arthritis three factors operate that may lead to total destruction of the joint—dissolution of matrix by leucoprotease and by excess plasmin, and the killing of the chrondrocytes by bacterial toxins.

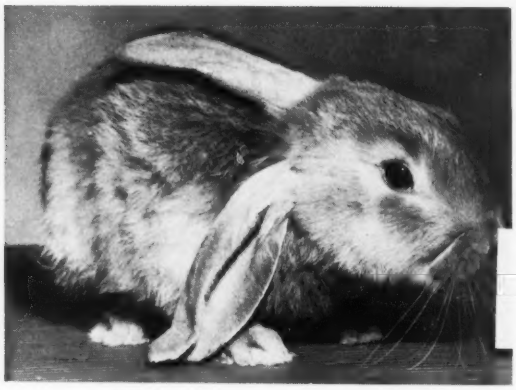

FIG. 7.—Rabbit 24 hours after intravenous injection of rabbit plasminogen. Right ear wiped over with chloroform to increase vascular permeability.

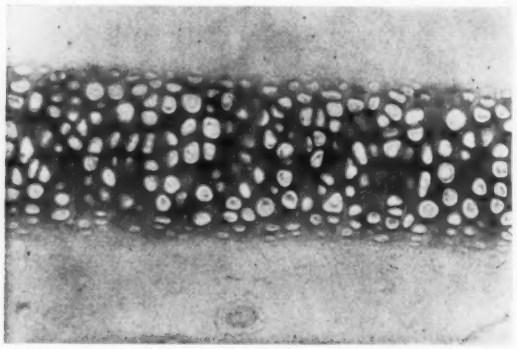

FIG. 8.—Ear cartilage of rabbit in Fig. 7 before treatment. (Azure A stain.)

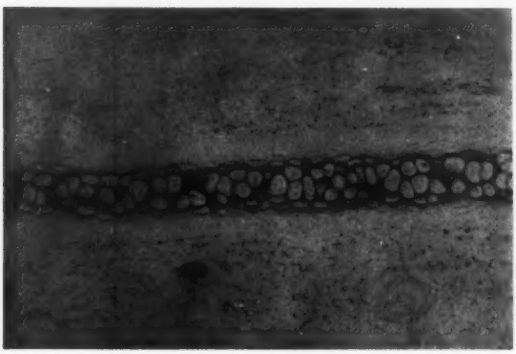

FIG. 9.—Ear cartilage of rabbit in Fig. 7 after treatment. (Azure A stain.)

FIG. 10.—Rabbit after 10 minutes' short-wave diathermy to right ear.

FIG. 11.—Rabbit 24 hours after partial right cervical sympathectomy. Note hyperaemia of right ear and curling of tip, indicating slight depletion of cartilage matrix.

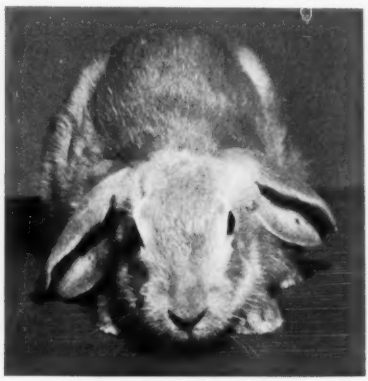

FIG. 12.—Rabbit 24 hours after intravenous injection of staphylokinase-activated plasmin.

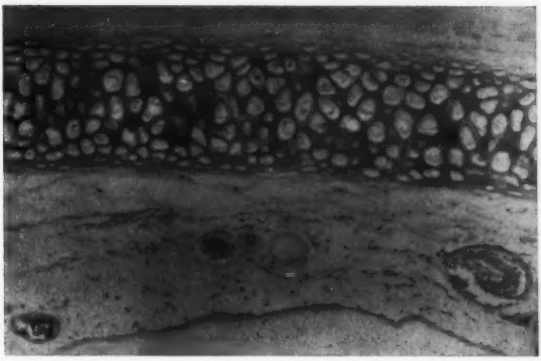

FIG. 13.—Ear cartilage of rabbit in Fig. 12 before injection of plasmin.

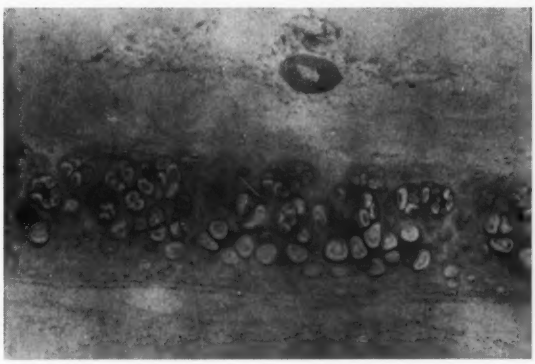

FIG. 14.—Ear cartilage of rabbit in Fig. 12 showing depletion of matrix by intravenous plasmin. (Azure A.)

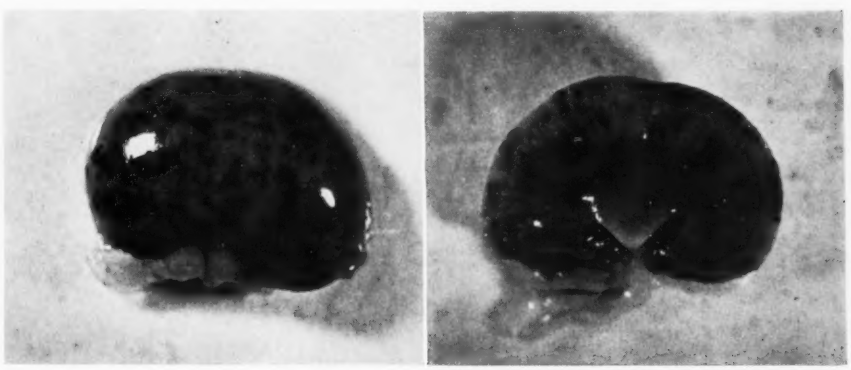

FIG. 15.—Kidneys of rabbit in Fig. 7, 30 hours after intravenous injection of plasminogen, showing multiple haemorrhages. (Formalin fixation.)

about 1 kg. in weight, are kept in cages on a standard diet of pellet food and greenstuff. All urine is voided into a polythene trough and is collected every 24 hours. Two 24-hour collections are made for the base-line level of glucuronic acid excretion before treatment, and subsequent collections are made until the level returns to base. Diagram 1 sets out graphically the rise in mg. per day of glucuronic

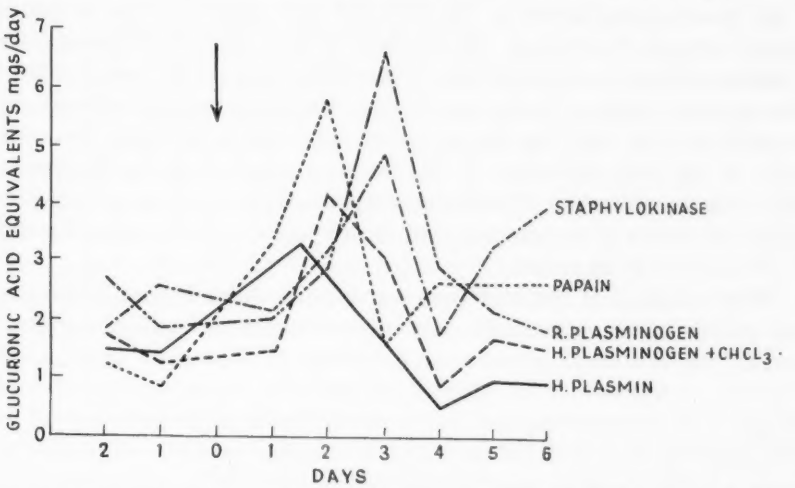

DIAGRAM 1.—Urinary excretion of carbazole-reactive material. Rabbits injected with different agents on third day, as indicated by arrow.

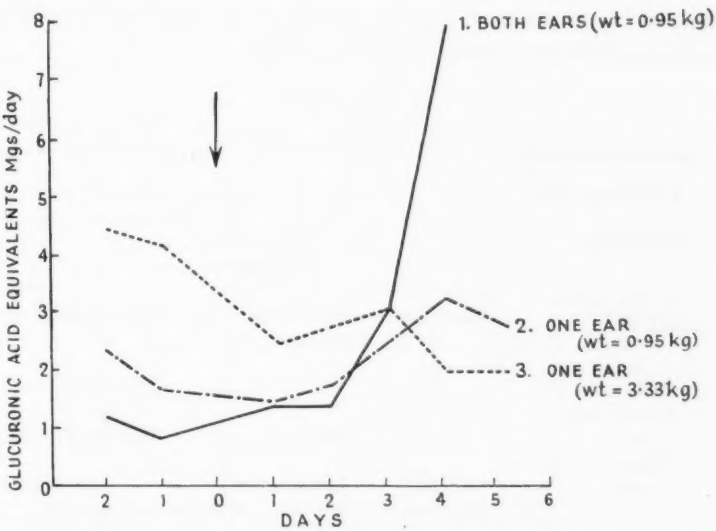

DIAGRAM 2.—Urinary excretion of carbazole-reactive material. Rabbits received infra-red treatment to one or both ears on third day, as shown by arrow.

acid equivalents following injections of the different enzymes, and details of these experiments are being published elsewhere.

It may be noted that, whereas chloroform applied locally to the ear greatly enhances the depletion of cartilage, the urinary excretion of mucopolysaccharide is not as high as that of plasminogen alone. This is almost certainly due to a hold-up of the mucopolysaccharide in the inflamed ear, where we find a gelatinous material around the cartilage. This material is also observed following infra-red or diathermy treatment to the ears. When litter-mates of the same weight were given infra-red treatment to the ears, one ten minutes on each side of one ear only, the other to both ears, the rise in mucopolysaccharide excretion was virtually double in the latter (Diagram 2). On the same graph is shown the absence of response in an old rabbit. Plasmin, like papain, does not produce such striking changes in mature rabbit cartilage, which presumably reflects some alteration in the constitution of its matrix.

When cartilage is removed from opposing articular surfaces there may be bony ankylosis; this is frequently the end-result of a suppurative arthritis. But when the matrix of cartilaginous tissue is depleted by plasmin the sequelae may be occult but no less serious. In many of the rabbits in which we have induced ear collapse we have found deposits of "fibrinoid" material in the glomeruli of the kidneys and in the heart. On one occasion multiple petechiae developed in the ears of a rabbit 24 hours after the intravenous injection of plasminogen, and at post-mortem examination six hours later severe tubular haemorrhages were found in the kidney (Plate III, Fig. 15). Sections show amorphous aggregates in the glomeruli and blood-vessels. Similar lesions have been described after intravenous administration of papain (Spicer and Bryant, 1958).

TABLE III

SUGGESTED MECHANISM OF "FIBRINOID" DEPOSITION

Provoking Agents	Blood	Cartilage
Vasodilators	Permeability enhancement	
Activators	Plasminogen → Peptides	Plasminogen + Tissue activator → Plasmin-Protein
Endotoxin + Leucocytes	Plasmin + Fibrinogen	
Streptokinase	"Altered Fibrinogen" + Chondroitin sulphate	← Chondroitin sulphate complex
	Fibrinoid	

Fibrinoid appears to be an insoluble complex of "altered" or "unclottable" fibrinogen combined with chondroitin sulphate, and is found as deposits on vessel walls and elsewhere in a variety of so-called "collagen diseases". A hypothesis for fibrinoid deposition is set out in Table III, though evidence for it will be published elsewhere.

SUMMARY

Though some agents may deplete cartilage by interfering with the synthesis of matrix or effecting the release of mucolytic enzymes from cells, the principal agents are leucoprotease and plasmin. These probably act in conjunction in suppurative arthritis.

When vascular permeability is sufficiently increased to allow plasminogen to pass from the blood to cartilage tissues, the plasminogen is activated *in situ* to plasmin, which splits the protein–chondroitin-sulphate complex of the matrix. The chondroitin sulphate leaches out into the blood and some is excreted in the urine. It also appears to precipitate with "altered" fibrinogen to form fibrinoid.

ACKNOWLEDGMENTS

I wish to acknowledge the generosity of the Nuffield Foundation in providing a grant for technical assistance, and of the University of London and the Peel Medical Research Trust, who have provided essential equipment. I would also like to thank our Medical Photographic Department and Mr. Derek Sayers for assistance with the photographs and sections.

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ORIGINAL PAPER

FUNCTION OF CERTAIN SHOULDER MUSCLES IN POSTURE AND IN HOLDING WEIGHTS

By J. G. BEARN

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Few studies on the function of the shoulder muscles during posture and static loading have been made. This paper describes electromyographic observations on the activity of the trapezius and also the muscles acting longitudinally across the shoulder-joint when supporting weights. Since these observations were made Davis (1959) suggested that in the erect posture weight appears to be transmitted to the pectoral girdle mainly by the deltoid, and to the trunk by the trapezius and other muscles. On the other hand, Basmajian and Bazant (1959) found no electromyographic activity in the longitudinal muscles acting across the shoulder-joint. They concluded that downward dislocation during weight-lifting was prevented by a locking mechanism due to the slope of the glenoid fossa, leading to the tightening of the superior part of the capsule and the coraco-humeral ligament, and also to the activity of the supraspinatus muscle.

METHODS

Forty-six male medical students took part in this investigation. The recordings were made with surface electrodes and a standard Ediswan electroencephalograph. This method is painless and does not disturb the muscles in any way. The electrodes were concave disks of silver 1 cm. in diameter, and were fixed in position with adhesive plaster. Before use the dome was filled with Cambridge electrolyte jelly. Recordings were taken from the upper fibres of the trapezius (the occipito-clavicular fibres), the anterior, middle, and posterior parts of the deltoid, the pectoralis major, the biceps, and the long head of the triceps. The recordings were made with the subject standing in a relaxed upright posture, first with the arms unloaded, then with symmetrical loading of the arms up to 25 lb. weight.

RESULTS

1. Trapezius

Most subjects showed slight activity in the upper fibres of the trapezius when recordings first started. Within one to two minutes this activity ceased, either spontaneously or when the subject was encouraged to relax and settle the shoulders into the most comfortable position. In four subjects persistent activity was found in this muscle.

With loading up to 10 lb., three-quarters of the subjects showed no activity in

the trapezius; the remaining one-quarter showing a low level of activity, compared with the great increase in activity when a minimal attempt was made to elevate the shoulders but without producing movement. When a 25-lb. weight was held two-thirds of the subjects showed a low level of activity as compared with the great increase which occurred when a minimal attempt was made to elevate the shoulders, the remaining one-third being able to relax the muscle completely. These subjects showed depression of the outer end of the clavicle up to an inch.

2. Deltoid, Biceps, Triceps, and Pectoralis Major

No activity was found in these muscles without loading of the arms. With loading up to 25 lb. some subjects showed initial activity, particularly in the deltoid. They were encouraged to relax, and within one to two minutes activity ceased in all the longitudinally acting muscles. The posterior fibres of the deltoid, however, showed persistent activity in most subjects.

DISCUSSION

1. Trapezius

Although it is usually assumed that the trapezius is responsible for maintaining the position of the scapula, this investigation shows that the upper fibres of the trapezius—i.e. the occipito-clavicular fibres—do not necessarily support the shoulder-girdle in the relaxed upright posture, and that even moderate weights may be held with no or little activity in this muscle. In these circumstances depression of the outer end of the clavicle occurred in many subjects. As a result it seems probable that the structures passing over the first rib, particularly the lower trunk of the brachial plexus, would be subjected to a much greater degree of tension than if the load were supported actively by the trapezius.

Telford and Mottershead (1948), in an extensive operative and anatomical study of pressure at the cervico-brachial junction, stated that many patients were seen during and after the war with paraesthesia of the upper limbs. They were almost entirely middle-aged women suffering from overwork and under-nourishment, forced to do unaccustomed heavy work, stand for many hours in queues, and carry heavy shopping baskets. These authors concluded that the paraesthesia was due to drag of the brachial plexus across the tendinous anterior edge of the scalenus medius, and that loss of tone in the shoulder-girdle muscles was an important contributory factor. Friedman, Argyros, and Steinbrocker (1959) reported that activities which tend to depress the shoulder, such as carrying heavy suitcases or other objects, are likely to intensify the symptoms in this condition. Lloyd (1948) found that rehabilitation of the shoulder muscles resulted in relief of symptoms in a high proportion of cases. Boulter (1959) has pointed out that this condition may be distinguished from the carpal tunnel syndrome by the distribution of the pain and paraesthesia. In the carpal tunnel syndrome the symptoms

are localized in the distribution of the median nerve, whereas in the costo-clavicular syndrome the lower trunk of the brachial plexus is most usually affected and the distribution of pain is therefore in the territory of the eighth cervical and first thoracic nerves.

It is suggested that the capacity for carrying weights without activity in the trapezius as shown in this investigation may be an aggravating factor in lesions at the cervico-brachial junction, and that weights should not be held unless the shoulder-girdle is actively supported by the trapezius.

2. Muscles Acting Longitudinally across the Shoulder-joint

This investigation further shows that moderately heavy weights (up to 25 lb.) may be held in the hands with no activity in the longitudinal muscles acting across the shoulder-joint. The load in these circumstances is borne by the capsule of the shoulder-joint, and particularly the coraco-humeral ligament. Basmajian and Bazant (1959) suggested that a locking mechanism occurred preventing downward dislocation. In the present investigation, when a 25-lb. weight was held to the limit of endurance some separation between the acromion and the greater tuberosity of the humerus was noted, and also in some subjects slight hollowing occurred between these two points, suggesting that some downward subluxation had taken place.

When weights are carried in this way considerable strain is thrown on the superior capsule of the shoulder-joint and the rotator cuff. Although in no sense "the cause" of lesions of the rotator cuff, this capacity for carrying weights with relaxation of the deltoid and the other muscles running longitudinally across the shoulder-joint may well be an aggravating, or possibly even an initiating, factor in this condition. It may be of significance that lesions of the rotator cuff are commoner in labourers and also in the right shoulder (Mattingly, 1960). It is therefore suggested that heavy weights should not be carried unless the shoulder-joint is actively supported by the deltoid.

The work reported in this paper provides further examples of the way in which anti-gravity muscles may be inactive when the subject is standing in a relaxed at-ease posture. Following the classic work of Sherrington on muscle tone it has been widely assumed that the upright posture in man is normally maintained by tonic muscular activity and not by tension in ligaments, which, being relatively inextensible, serve to stabilize a joint only at the limit of movement (Wiles, 1959). More recent investigations have shown that this view no longer necessarily holds. Joseph and Nightingale (1954) and Joseph and Williams (1957) have shown that, provided the subject is standing in a relaxed at-ease position, the postural muscles supporting the hip-, knee-, and ankle-joints show no electromyographic activity, except for continuous activity in the calf muscles. These joints are not in a balanced position, the plane of the centre of gravity of the body running just behind the hip-

joint and in front of the knee- and ankle-joints, with the result that these joints are tending to hyperextend under the pull of gravity. Smith (1954a, 1956, 1957) has shown that the stability of these joints in the relaxed at-ease posture is dependent on the tension of their ligaments and also the deep fascia round them. In the case of the ankle-joint, however, this mechanism is not adequate, since the centre of gravity falls well in front of the joint, and continuous activity in the calf muscles is essential to stabilize this postural level.

Similarly, it has been shown that in the at-ease position the muscles normally regarded as supporting the arches of the foot are inactive (Basmajian and Bentzon, 1954) and that the plantar aponeurosis and plantar ligaments are supporting the body weight in this posture (Hicks, 1954).

It must not be concluded, however, that standing in a posture with little or no muscle activity is ideal. Smith (1954b) has suggested that if the resulting stress on the passive supporting tissues exceeds a certain limit damage could result, which would become progressively worse over the years, and would also delay recovery after injuries to the joint tissues. As Wiles (1937, 1959) has emphasized, a dynamic approach to posture is essential, which is not concerned just with strengthening muscles, but with developing "new postural reflexes . . . to keep a good posture during every variety of movement".

It is, however, unlikely that we ever stand "at ease" for long. Hellebrandt (1938) showed that during standing one is continually swaying backwards and forwards—"movement on a stationary base"; and Smith (1954b) further showed, in a study of people standing in bus queues or at railway stations, that one stance is never held for more than 30 seconds, on the average, before changing to another stance. One might speculate that this change in posture is a protective reflex due to the tension in the postural ligaments, and it is well known that patients with congenital indifference to pain may develop a progressive disorganization of their joints similar to that found in Charcot's disease (Houwen, 1961).

The anatomical aspects of this investigation have been published in detail elsewhere (Bearn, 1961).

SUMMARY

Electromyographic recordings are reported from the upper fibres of the trapezius, the anterior, middle, and posterior fibres of the deltoid, the clavicular head of the pectoralis major, the biceps, and the long head of the triceps, using surface electrodes and an Ediswan electroencephalograph, with the arms unloaded, and with the arms loaded up to 25 lb. With the arm unloaded, no electromyographic activity was found in any of the muscles studied. With loading up to 10 lb. no activity was found in the muscles acting over the shoulder-joint. The trapezius showed a low-grade intermittent activity in one-quarter of the subjects, the remaining three-quarters showing complete relaxation after two minutes. With loading up to 25 lb., again no activity was found in the muscles acting

longitudinally across the shoulder-joint, except for the posterior fibres of the deltoid, which showed a low-grade activity in the majority of subjects studied. The trapezius muscle showed a low-grade activity in two-thirds of the subjects, the remaining one-third showing no electromyographic activity.

Attention is drawn to the potential dangers of holding weights with little or no activity in the muscles supporting the shoulder-joint and the shoulder-girdle.

Acknowledgments

The author is indebted to Professor E. W. Walls for his interest in this investigation, to the late Professor Samson Wright for allowing the use of equipment in his department, to Dr. W. F. Floyd for his guidance, and to the medical students who so willingly took part in this study.

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ORIGINAL PAPER

THE SPIROGRAM IN ANKYLOSING SPONDYLITIS

THE "REVERSED EMPHYSEMA" SIGN

By B. H. BASS and W. G. WENLEY

From the London Hospital, Whitechapel

In recent years recognition of the early symptoms of ankylosing spondylitis has led to earlier diagnosis of the condition (Baird *et al.*, 1955; Hart, 1955). The initial radiological changes in the sacro-iliac joints, however, may still be difficult to assess, particularly in adolescents.

In this paper we describe a new, simple aid to the diagnosis of ankylosing spondylitis by means of spirometric analysis of breathing patterns.

METHOD

A low-resistance spirometer (Bernstein and Mendel, 1951) and kymograph set to rotate rapidly at a speed of 250 mm. per minute was used in all cases. Patients were instructed to hold the facepiece tightly against their faces and to take three successive rapid and deep breaths, in and out, through the mouth. The time taken in explaining the method and for the performance of the test amounted to less than three minutes for each patient. The spirogram obtained in this way was then analysed, and the maximum inspiratory and expiratory flow rates were measured from the slope of the tracing.

RATIONALE

In health the inspiratory and expiratory slopes are very steep. The maximum inspiratory flow rate (M.I.F.R.) and the maximum expiratory flow rate (M.E.F.R.) are in the order of 400–600 litres per minute. In emphysema, where there is airway obstruction to expiration, the M.E.F.R. is much reduced, so that the expiratory slope on the tracings is more gentle. Inspiration is less affected, and values for the M.I.F.R. are near the normal (Fig. 1).

One of us (B. H. B.) had noticed an empirical change in the shape of the spirogram obtained in the routine performance of lung-function tests on patients with ankylosing spondylitis. The changes consist in a reversal of those encountered in emphysema as described above. The expiratory slope is much like the normal, but the M.I.F.R. becomes reduced, giving a relative slowing of inspiration in relation to expiration. This is singular and gave rise to the name of "reversed emphysema" sign. We have observed this pattern in 18 of 20 cases of ankylosing spondylitis tested. By contrast, no patient with rheumatoid arthritis has shown this spirometric pattern.

RESULTS

Twenty patients in all stages of ankylosing spondylitis were investigated. All had been examined clinically and radiologically. In each case there were complaints of backache and stiffness of varying degrees, and radiological features ranged from the early changes of sacro-iliitis to a fully developed "bamboo" spine. The chest expansion was measured in each case and was never more than 2 inches, though this does not correlate well with the state of lung function (Zorab, 1960). Spirometry was carried out in every case at the same time of day

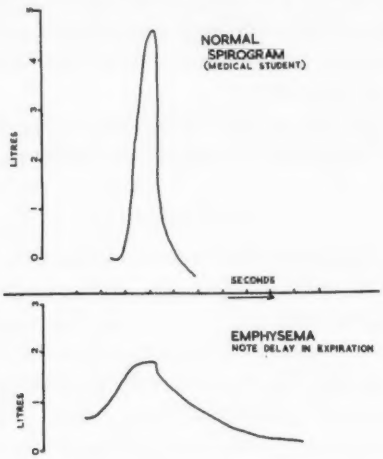

FIG. 1

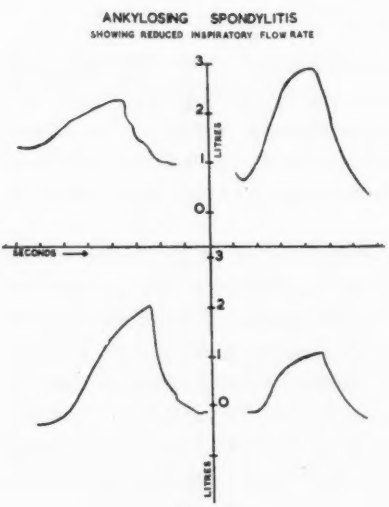

FIG. 2

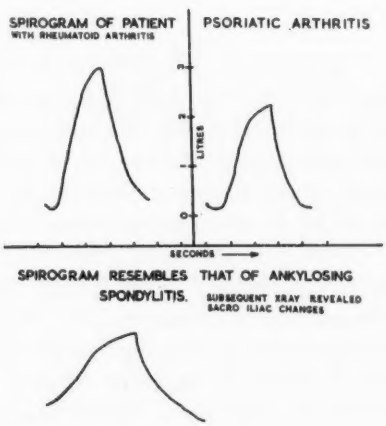

FIG. 3

(early afternoon) in order to eliminate any error arising from the known tendency of spondylitic joints to be most stiff in the early morning. Seven patients with definite rheumatoid arthritis according to the American Rheumatism Association criteria (Ropes *et al.*, 1956) were also assessed clinically and spirometrically. The tracings from 11 cases of emphysema were recorded to offer a contrast and to act as a control. Representative tracings are reproduced (Figs. 1–3), including a normal one obtained from a healthy medical student. Maximum

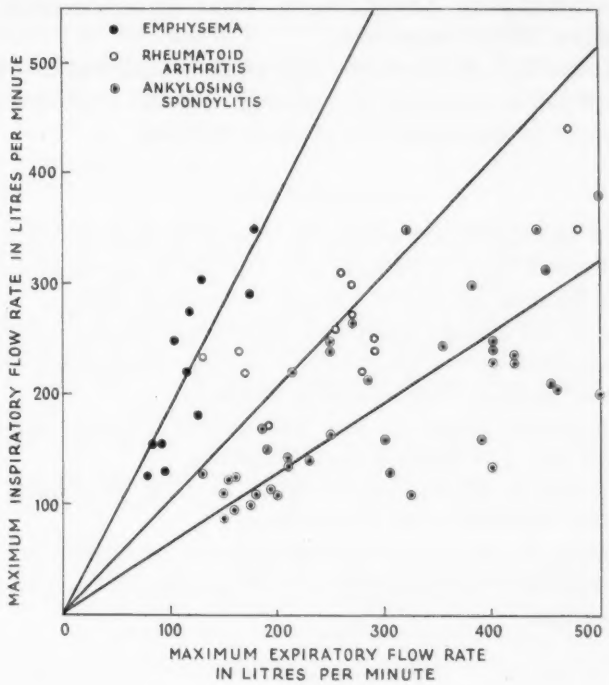

FIG. 4

inspiratory flow rates were plotted against maximum expiratory flow rates and the average for the three diseases was plotted on one graph (Fig. 4). From this it can be seen that the slope for ankylosing spondylitis is the flattest. As could be predicted, the slope for emphysema is much steeper because of the relative sparing of the M.I.F.R. Rheumatoid arthritis comes between the two, fitting into the normal so far as flow rates are concerned and standing discrete from the group with ankylosing spondylitis.

DISCUSSION

Involvement of the costo-vertebral joints plays an important part in ankylosing spondylitis and provides a clue to the explanation of our findings.

Such involvement may precede sacro-iliac disease (Golding, 1955), though radiology of the costo-vertebral joints is a difficult and unrewarding procedure. One of the patients, whose spirogram is reproduced as an example of ankylosing spondylitis, presented with psoriasis of skin and toenails and a painful ankle followed shortly by low backache. She was thought to be suffering from psoriatic arthritis, but, consequent upon finding a spirogram so suggestive of spondylitis, radiographs of her sacro-iliac joints revealed characteristic changes. Radiographs of her costo-vertebral joints showed erosions. This is the only example of atypical spondylitis (Sharp, 1957) in our series.

It is suggested that this diagnostic test, which is rapid and easy to perform, should be employed as an adjunct to radiology, and that a spirometer could be used to advantage in departments of physical medicine.

SUMMARY

Maximum inspiratory and expiratory flow rates were calculated from the spirograms obtained from 20 patients with ankylosing spondylitis, 11 cases of pulmonary emphysema, and seven cases of rheumatoid arthritis.

Patients with ankylosing spondylitis showed impaired inspiratory flow rates; those with emphysema showed characteristic slowing of expiration, while patients with rheumatoid arthritis were relatively unaffected.

Plotting maximum inspiratory flow rates against maximum expiratory flow rates graphically served to delineate the three groups.

Early involvement of the costo-vertebral joints in ankylosing spondylitis appears to be the explanation for these findings.

It is suggested that the spirogram constitutes a simple diagnostic test for early ankylosing spondylitis which may well be more sensitive and accurate than early radiological changes.

ACKNOWLEDGMENTS

We thank Dr. W. S. Tegner and Dr. R. M. Mason for their encouragement in this work, also their patients whose willing co-operation made it possible.

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ORIGINAL PAPER

CHRONIC TENOSYNOVITIS OF EXTENSORS OF HAND AND FINGERS ("COMPOUND DORSAL GANGLION")*

By J. C. F. LLOYD WILLIAMSON

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SIMPLE ganglion on the back of the wrist and hand is a very common condition and, although treatment is notoriously unsatisfactory, diagnosis appears to be transparently obvious, for all other soft swellings in this region are by comparison rare. When, therefore, they do occur they are often unrecognized.

On the volar aspect of the wrist chronic flexor tenosynovitis, which can nearly always be proved tuberculous, even if uncommon, is well known under its old name of compound palmar ganglion and readily diagnosed. But a similar condition on the dorsum, chronic extensor tenosynovitis, which might also be termed compound dorsal ganglion, is, however, rare and its aetiology less clear-cut, while its documentation is relatively scanty. It is therefore not surprising that in some cases at first the true nature of the swelling is missed.

Chronic tenosynovitis of the extensors of the wrist is hardly mentioned in standard British textbooks of surgery.

Pulvertaft (1949) makes it clear that, while in the large majority of cases the flexor sheaths are involved, tenosynovitis also occurs in connexion with the extensor tendons of the dorsum of the wrist and hand, and sometimes too in the foot and ankle.

Iselin and Vassitch (1952) give a good description of all types of chronic tenosynovitis, as do Adams, Jones, and Marble (1940), Bickel, Kimbrough, and Dahlin (1953), and Mason (1934), but in all these series the total number of cases is relatively small and the incidence of extensor tendon lesions averages but 20% of this total.

I myself have seen 14 cases of chronic extensor tenosynovitis of the wrist in 15 years. As some cases were bilateral or multiple the total number of lesions was 20.

Undoubtedly chronic tendon-sheath infection is rare. Only 36 cases of tuberculous tenosynovitis of all types were seen in 45 years at Massachusetts General Hospital (Adams *et al.*, 1940) and 52 in 35 years at the Mayo Clinic (Bickel *et al.*, 1953). These included a number proved histologically or bacteriologically and others by clinical impression. It is interesting to note that in cases proved to be tuberculous, extensor lesions are few. In other words, tenosynovitis of the flexor tendons usually gives the typical and well-recognized picture of tuberculous

* Paper read at the Provincial Meeting of the British Association of Physical Medicine, Brighton, October, 1960.

compound palmar ganglion, and this can generally be proved histologically, but a lesion of the extensor tendons is relatively rare and its tuberculous nature often impossible to prove; it is perhaps more variable in degree and certainly less well recognized.

DIFFERENTIAL DIAGNOSIS

When the condition is well established the diagnosis is obvious, and, if loose bodies are present, crepitus is often felt. In the early stages there is more difficulty. The picture is one of insidious onset of a painless or moderately painful swelling along the line of the tendon, with to-and-fro fluctuation if a ligament crosses it. In the earliest cases the swelling may be obvious only if the patient tenses the back of the wrist (Plate IV, Fig. 1).

Simple ganglion is not infrequently the label given to a case of chronic tenosynovitis. Owing to the rarity of this dorsal tenosynovitis, and conversely the everyday finding of the simple ganglion, particularly on the back of the wrist, many cases are erroneously diagnosed and so treated as simple ganglion, by inadequate removal or by injection. Although occasionally the tumour may be tense and globular (like a typical simple ganglion), its elongated shape and flaccid or fluctuant consistency on examination (Plate IV, Fig. 2) and the appearance at operation (Plate IV, Figs. 3 and 4), if missed before, should point the way to the correct diagnosis.

Other lesions can on rare occasions be confused with the condition. Bunnell (1948) gives a concise list of these.

Traumatic tenosynovitis gives a short and typical history.

Pyogenic, syphilitic, and gonococcal tenosynovitis are rare, but as a rule diagnosis presents no difficulty.

Angioma is characterized by changes in size, which varies with position of limb and by compression.

Pseudoxanthoma (synovioma of tendon sheath) is distinctly uncommon, but can be misleading; it is usually firmer and more discreet, and before operation it may be mistaken for a large simple ganglion.

Lipoma of the hands and feet, though rare, when met with can closely simulate a tendon-sheath lesion. I recently saw a case which I thought was an example of chronic tenosynovitis of the extensor hallucis, a condition which has in fact been seen in another patient. Clinically it gave the impression of lobulation and fluctuation, but the case proved to be one of lipoma.

SEX AND AGE

In my own series of patients, 8 out of 14 were males and, including one man of 75 and one girl of 15, the average age was 42 years. Other series show slightly more men than women and an average age of about 30–40.

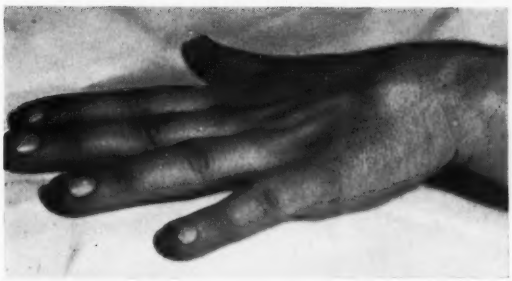

FIG. 1.—Left hand, early case involving common extensor tendons, showing swelling of tumour made obvious by tensing back of wrist.

FIG. 2.—Left hand, advanced case, showing swelling of tumour involving common extensor tendons above and below wrist.

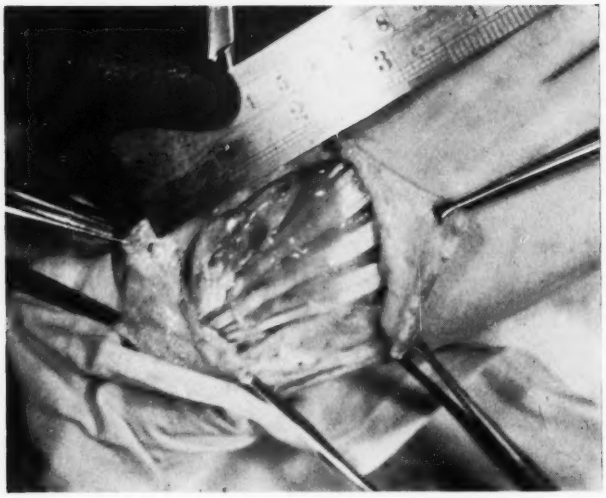

FIG. 3.—Left hand, early case involving common extensor tendons, at operation. Thin transparent veil, of salmon-pink hue, covering tendons.

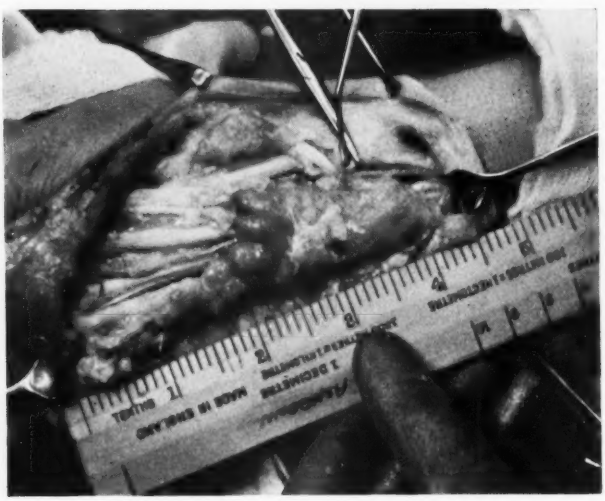

FIG. 4.—Left hand, advanced case, showing tumour extending from above wrist and over all common extensor tendons, most marked over tendon to fifth finger. Dorsal retinaculum has been divided. Numerous sago bodies found within sheath.

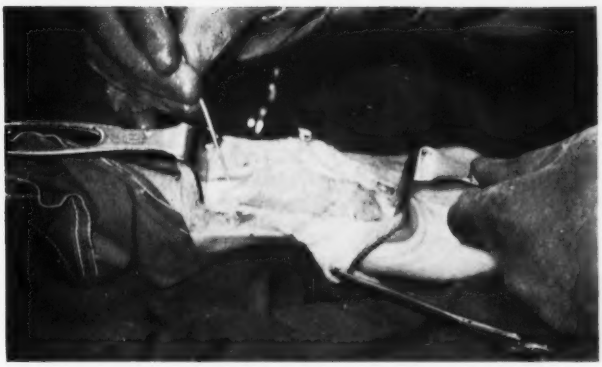

FIG. 5.—Left hand, advanced case involving extensor carpi ulnaris.

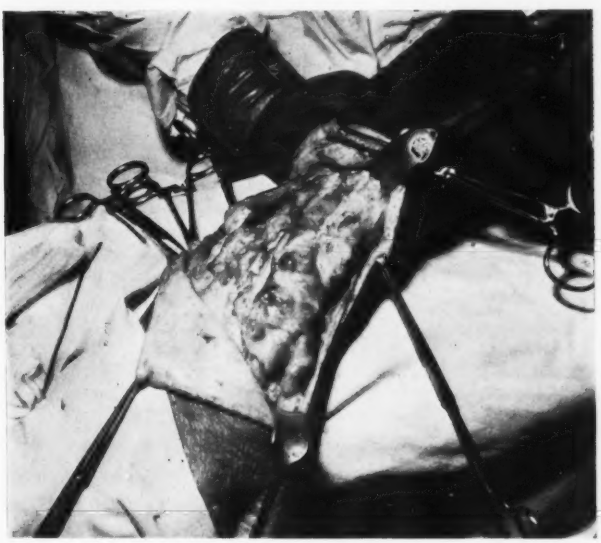

FIG. 6.—Right hand, lesions involving extensor pollicis longus and extensor carpi ulnaris.

SIDE OF LESION AND TYPE OF PATIENT

Chronic extensor tenosynovitis occurs rather more commonly in the right hand than the left. In my own series 10 lesions were on the right and 7 on the left.

While the condition can occur in children, Pulvertaft states that the patient is usually an adult male and often a cowman or butcher. Bunnell supports this. According to Adams and his colleagues (1940), Wiles (1949), and others heavy manual workers are most commonly affected, and this is true of my own series: all the men were, or had been, manual workers, but only one had any possible bovine contact.

COURSE OF DISEASE

In my own cases there was a history of insidious onset of swelling over three months to ten years (mean four years) and two patients had had previous operations for removal of so-called simple ganglia. A minority had no pain or stiffness, but in most cases pain was slight or moderate, persistent, worse with use of the hand, and accompanied by some stiffness. There was no clear evidence of trauma as a predisposing factor, and this is a general finding.

The condition is most usually due to infection of the common extensor digital sheath (Plate IV, Figs. 3 and 4), but lesions of other tendons are not infrequent. Plate IV, Fig. 5 shows involvement of the extensor carpi ulnaris, and Fig. 6 involvement of the extensor carpi ulnaris and extensor pollicis longus. Lesions of extensores carpi radiales and extensor indicis proprius have also been met with.

The tendons involved in my own series were as follows:

Common extensors of fingers	12
Extensor pollicis longus	4
Extensor carpi ulnaris	2
Extensores carpi radiales	1
Extensor indicis proprius	1
Total lesions	20

In addition similar chronic tenosynovitis was found in the extensor hallucis longus, the tibialis anterior, and the flexors of the toes.

The area involved was fairly constant in all lesions of the common extensor tendons, and the ganglion extended from the distal third of the dorsum of the hand upwards under the dorsal carpal ligament to just above the wrist.

The macroscopic appearance was interesting; the "ganglia" had in each case a pink, fleshy, "meaty" look, but varied greatly in thickness. The most advanced case had a thick mass and rice bodies (Plate IV, Fig. 4), while Plate IV, Fig. 3 shows an early case with a very thin transparent veil which was of a beautiful salmon-pink hue.

In every case the "ganglion" lay between the skin and the tendons and

ensheathed each of them like a glove; sharp dissection was needed to remove it from the tendons. In most cases the tendons appeared perfectly healthy, but in two cases early infection and fraying were seen.

PATHOLOGY

Although chronic tenosynovitis, particularly of the extensor tendons, can often not be proved to be tuberculous, it would seem certain that (possibly with very few exceptions) all cases are in fact of tuberculous origin. This is supported by the case of a woman who, in 1956, presented with a typical compound palmar ganglion on the right together with right and left compound dorsal ganglia, for which three excision operations were performed. Histology of the palmar ganglion showed epithelioid and giant cells, but neither of the dorsal lesions showed similar changes.

The pathology of tuberculous tenosynovitis runs a fairly typical course. The tendon sheath becomes slowly thickened and distended by serous exudate; after a variable time, usually several years, fibrin appears followed by melon-seed or rice bodies. Although there is often matting of the two layers of the sheath with partial or complete obliteration of the sheath space and also thickening of the visceral as well as the parietal layer, the tendon itself can still be dissected out, and shows little or no pathological change unless the disease is very advanced. Finally tendon infection and rupture may occur. These appear to be much more common in France and the U.S.A. than in Great Britain.

Iselin and Vassitch (1952) describe a series of 34 patients which seems to include many very advanced cases, for in 17 of the 34 cases tendon involvement (14 flexor and 3 extensor) was found. Mason (1934) gives a similar percentage involvement (12 out of 23). The first-mentioned authors claim that after two years' infection tendon destruction is probable, and after three years certain.

HISTOLOGY

Histological examination shows a rather ill-defined picture which has no resemblance to that of simple ganglion.

Dr. R. W. P. Johnson has reviewed the sections of all my cases and summarized the results. The general picture was one of infiltration to a greater or less extent by chronic inflammatory cells. Lymphocytes predominated in all cases, but plasma cells were also frequent and polymorphs and eosinophils were occasionally seen. In many cases no giant cells or tuberculoid lesions were found, and in these cases there was no positive evidence of tuberculosis. In some cases there was endarteritis. In only two cases were epithelioid and giant cells seen. In no case could acid-fast bacilli be demonstrated or cultured, and inoculation of guinea-pigs, when carried out, was also negative.

It is in fact generally agreed that a diagnosis of tuberculous tenosynovitis can

often not be made by the pathologist on the histological findings, and even culture and guinea-pig inoculation may give no proof.

TREATMENT

Pre-operative Splintage and Sanatorium Treatment

This has been suggested by Pulvertaft and others, but in view of the apparent unimportance of the condition, coupled with the relative triviality of the symptoms, it is felt that with the ordinary form of the disease few patients are likely to agree to this and in the average case it may not be necessary. In advanced cases, however, these measures might well be valuable adjuncts to surgery.

Surgery

Surgery, it is generally agreed, is the first line of attack. It must be carried out with a bloodless field and considerable patience. A meticulous removal of the affected tissue is essential; as this passes all round the tendons and is in close contact, removal is rather piecemeal and tedious and has to be by sharp dissection. The dorsal carpal ligament must be divided and later reconstituted. None the less, excision is considerably easier than with the compound palmar ganglion. In any operation for compound dorsal ganglion Mason advises exploration of the sheaths of the extensores pollicis and abductor pollicis longus, as he states these are always involved. Early post-operative movements are essential if stiffness and loss of function are to be avoided. In my own cases I support the limb after operation with a dorsal plaster slab splint, but finger movements are encouraged from the first. The plaster is removed daily for physiotherapy and is soon discarded entirely.

Surgery alone can cure, but not infrequently recurrence takes place, even if excision has been as thorough as possible.

DEEP X-RAY THERAPY

This is thought by some to be a valuable ancillary: Bunnell follows up excision with irradiation. Some early cases in his series remain satisfactory after surgery followed by irradiation alone; in others, however, there was a recurrence.

ANTITUBERCULOUS DRUG THERAPY

Treatment with antituberculous drugs is certainly a valuable adjunct to operation and is now given to every case. The length of the course should be at least three months, but longer in advanced cases. For choice it should be started before and continued after operation. Some patients will not, however, tolerate it.

Iselin and Vassitch (1952) advocate medicinal therapeutic measures alone in early cases, but Bickel *et al.* (1953) report poor results with purely conservative measures.

To sum up, with our present knowledge it seems clear that the most promising

line of treatment in these cases is meticulous surgery together with administration of antituberculous drugs, and it is possible that further developments along these lines may make it safe to rely solely on drug therapy to the exclusion of surgery.

REPAIR OF TENDON LESIONS

Iselin and Vassitch discuss in detail the treatment of tendons stretched or ruptured as a result of this disease. In brief, plication, shortening by excision of a section, and grafting are advocated as the lesion demands, and in comparison with traumatic cases the results are surprisingly good. Repair of extensors is still more functionally satisfactory than that of flexors.

PROGNOSIS

This is not easy to assess as the disease varies greatly in virulence and speed of spread. It is a potentially serious disease, with tendencies to recurrence and to tendon damage. In France and the U.S.A. more cases seem to be of the severe type than in Britain. As one would expect, in patients with low-grade infection the onset is slower and they seek advice only after perhaps three or four years; these cases do better with treatment than those running a faster course. It is possible that lesions of the extensor sheaths carry a better prognosis than those of the flexor sheaths, and this may be due to several factors. Swellings on the dorsum of the hand are more superficial and therefore more obvious than volar ones, and so are reported and treated sooner; also excision is mechanically much easier on the dorsum. There is no doubt that histological proof of tuberculous infection is less common with extensor than with flexor lesions.

Adequate treatment carries a fair prognosis of cure with little loss of tendon function, for if recurrence does not supervene movements are usually excellent. Recurrence is, however, relatively common; Iselin and Vassitch had 11 recurrences out of 17 operations followed up, Bunnell 6 out of 14, and Bickel *et al.* 7 out of 30. In my own series the recurrence rate was 4 out of 14, and 3 of these were in the first 4 cases. In the last 10 cases, operated on since 1952, there has been only one recurrence, and it is interesting to note that in the majority of these cases surgery has been combined with antituberculous drug therapy. The disease may reappear in sheaths already treated, or other sheaths may become infected; thus the first lesion may be dorsal and the "recurrence" palmar.

As in primary infection, so in recurrence, the outlook is worse if it soon follows treatment and, according to Iselin and Vassitch, if the recurrence appears in spite of the pre- and post-operative use of streptomycin. The prognosis in treated cases of recurrence seems to be as good as in primary cases.

Recurrence may take place after many years. For this reason, and because of the difficulty of assessing the severity of the infection, the prognosis must be guarded, and a close and prolonged follow-up is imperative.

SUMMARY

A series of 14 cases of chronic tenosynovitis of the extensor tendons of the wrist and hand is reported.

Chronic infection of the sheaths of the extensors of the wrist and hand is relatively rare; it is insidious in onset, and diagnosis is often delayed. It occurs chiefly in adults doing heavy manual work, and males are more often affected than females. Although most, if not all, cases are probably of tuberculous origin, histological or bacteriological proof is less frequent and later than with flexor lesions. However, treatment is usually sought rather earlier and the relative prognosis is somewhat better.

Surgical excision is the first line of treatment. Antituberculous drug therapy appears to be of value as an aid to surgery, and may in time supplant it.

If recurrence does not ensue the functional results are generally good. Recurrences are, however, common and should be treated on the same lines as primary infection. The prognosis seems to be no worse than with primary cases.

ACKNOWLEDGMENTS

I am much indebted to Dr. E. Millington for his radiological advice and treatment, to Dr. A. Macfarlane for his help with the antituberculous therapy, and to Mr. L. W. Lauste, Dr. E. W. Lindeck, and Dr. H. S. Fleming for referring cases to me. I have received valuable assistance with the pathology from the late Dr. L. R. Janes, and from Dr. R. W. P. Johnson, who has recently reviewed the histology in all the cases and summarized the findings. My thanks are also due to the Brighton and Lewes Hospital Group clinical photographers, Mr. S. T. Higgins and his predecessors, for the excellent photographs.

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ORIGINAL PAPER

THE PROGNOSIS AND MANAGEMENT OF SOME MUSCULAR DISEASES*

By JOHN N. WALTON

From the Newcastle General Hospital and Royal Victoria Infirmary, Newcastle upon Tyne

INCREASING interest has been taken in recent years in the diagnosis and management of many diseases of muscle. As in so many fields of medicine, increased knowledge of muscle disease has brought with it many new problems of understanding and interpretation and of classification, and many of the advances which have been made in our knowledge have added complexity rather than clarity. One has only to look at the endocrine and metabolic myopathies, for instance, whose number is being added to almost daily, to realize how complicated the situation has become. I cannot hope to cover the whole field within the limits of a short paper, but I propose to consider certain of the commoner varieties of muscle disease with particular reference to prognosis and management. I shall exclude from consideration the large and interesting group of congenital myopathies, some of which produce or are associated with infantile hypotonia, and shall concentrate on progressive muscular dystrophy and related disorders, polymyositis, myasthenia gravis, and some of the commoner metabolic myopathies.

Before doing so I think a word about terminology is necessary. Some confusion has arisen concerning the use of the terms "muscular dystrophy" and "myopathy". In particular, the utilization of the term "muscular dystrophy" to describe several varieties of naturally occurring myopathy in animals, as well as the type of myopathy which can be produced experimentally in animals as a result of tocopherol deficiency, has been unfortunate, as it has led in certain quarters to the assumption that this condition is related to the human inherited disorder bearing the same name. They are, in fact, quite different; it should, however, be mentioned that within the last few years two varieties of muscular dystrophy occurring in the animal kingdom, one in mice and the other in chickens, have been shown to be inherited and are probably more closely related to the human disease. In my own view the term "myopathy" can be used for any disease in which the symptoms and signs clearly indicate the presence of a structural, biochemical, or electrical disorder involving the muscle fibres themselves or the intramuscular connective tissue, without involvement of the peripheral nerves or central nervous system. "Muscular dystrophy", on the other hand, should be reserved for the inherited disease occurring in man or in animals, and can be defined as "genetically determined, primary, degenerative myopathy".

* Paper read in a symposium on "Diseases of Muscle" at an Advanced Course of the British Association of Physical Medicine, London, April 20, 1961.

PROGRESSIVE MUSCULAR DYSTROPHY

While it is no part of my task to consider in detail the clinical features, diagnosis, and genetic aspects of this condition, it is impossible to discuss prognosis and management without reference to classification, as the one depends so much upon the other. In this group of cases one may first distinguish two broad groups—namely, the "pure" muscular dystrophies on the one hand, and cases with myotonia on the other. The "pure" muscular dystrophies can in turn be classified into five principal groups—namely, the Duchenne (pseudo-hypertrophic), limb-girdle, facio-scapulo-humeral, ocular, and distal forms (Walton, 1961). Of these, the first three groups are much the most common. From the information which has been collected in many parts of the world during the last few years it is possible to outline with a fair degree of accuracy the clinical and genetic characteristics of each of these varieties of the disease.

Duchenne-type Dystrophy

The Duchenne type of dystrophy is characterized by: (*a*) expression usually in the male but occasionally in the female; (*b*) onset usually in the first three years of life, but occasionally as late as the third decade; (*c*) transmission as a sex-linked recessive character in the majority of cases, but as an autosomal recessive in up to 10%; (*d*) symmetrical involvement first of the pelvic girdles, later of the shoulder girdles; (*e*) pseudo-hypertrophy, particularly of the calf muscles, but sometimes also of the quadriceps and deltoids, in 80% or more of cases; (*f*) steady and rapid progression in most instances, leading to inability to walk, usually within ten years of the onset; a proportion of cases of this clinical type are more benign and the progress of the disease is substantially slower, though severe disability eventually results; (*g*) progressive deformity with muscular contractures and skeletal distortion and atrophy occur; (*h*) death from inanition or respiratory infection occurs often in the second decade, but since the widespread use of antibiotics it has been delayed in a proportion of cases until middle life.

The term "Duchenne" as used to identify the common rapidly progressive type of the disease, which affects principally young boys, is to be preferred to the more traditional term "pseudo-hypertrophic" in view of the fact that pseudo-hypertrophy of muscle can occur in all the varieties of muscular dystrophy, though it is admittedly much more frequent in cases of the Duchenne type.

Limb-girdle Type

The limb-girdle type of dystrophy is characterized by: (*a*) expression in either sex; (*b*) onset usually late in the first or in the second or third decades, but occasionally in middle age; (*c*) transmission as an autosomal recessive character in most instances, but occasionally as an autosomal dominant; (*d*) primary involvement of

either the shoulder-girdle or the pelvic-girdle muscles, with spread to the other after a variable period; (*e*) muscular pseudo-hypertrophy occurs in a proportion of cases, but is uncommon; (*f*) abortive cases are uncommon; (*g*) there is variable severity and rate of progression of the disease; (*h*) most patients become severely disabled in middle life and die before the normal age.

Facio-scapulo-humeral Dystrophy

The facio-scapulo-humeral type of dystrophy is characterized by: (*a*) expression in either sex; (*b*) the disease begins at any age from childhood until late adult life; (*c*) the condition is inherited usually as an autosomal dominant character, but occasionally as an autosomal recessive; (*d*) abortive or mildly affected cases showing arrest of the disease are common; (*e*) the condition affects first the face and shoulder-girdle muscles, but subsequently spreads in most cases to the pelvic girdle; (*f*) muscular pseudo-hypertrophy is very uncommon; (*g*) the progress of the disease is insidious, with prolonged periods of rest, and, although a small proportion of cases occur in which the disease process is comparatively rapid, most patients survive and remain active to the normal age; (*h*) muscular contractures and skeletal deformity are comparatively uncommon.

Ocular and Distal Types

The other two varieties of "pure" muscular dystrophy—namely, the ocular and distal types—are considerably more rare. The ocular variety, which was first described by Hutchinson in 1879 and by Fuchs in 1890, was fully reviewed by Kiloh and Nevin in 1951. In this type of muscular dystrophy the disease begins in the external ocular muscles and gives rise to bilateral ptosis and a gradually increasing ophthalmoplegia. Commonly there is also weakness of the orbicularis oculi and sometimes of the other facial muscles, while dysphagia and some involvement of muscles around the shoulder-girdle is seen in a proportion of cases. In some families there is clear evidence that the disease is inherited, but a great many cases are sporadic. The exact relationship of this form of muscular dystrophy to the other varieties remains obscure, and it seems that for the present at least it should be regarded as a separate and independent entity. The same is true of the distal form, which, though rare in Great Britain, is common in certain parts of Sweden, and Welander in 1951 was able to review well over 240 cases. In her experience the disease began in the small muscles of the hands and of the feet and spread proximally, but it was, on the whole, benign and slowly progressive and tended to begin in late adult life or even in middle life. The five cases I have seen personally in Britain were all sporadic, though the disease followed a similar pattern to that described by Welander. In her series, however, the condition was clearly inherited by an autosomal dominant mechanism.

Treatment

When one comes to consider the treatment of muscular dystrophy it is impossible not to be somewhat despondent. I think it would be true to say that there is no treatment available at the present time which has any real influence on the course of the disease. The difference in the natural history of the illness in the various types must, however, be accepted in view of the fact that some forms of the disease are much more benign than others. So far as drug therapy is concerned, a great many remedies have been claimed from time to time as being of benefit, but have been shown by subsequent study to be of no real value. To give a number of examples, glycine, vitamin E and many of its chemical analogues, multiple amino-acid therapy, and even neostigmine, along with many other remedies, have been advocated enthusiastically from time to time, but none of these drugs has any real value, save for the fact that in a very small proportion of cases of otherwise typical muscular dystrophy some temporary benefit can be derived from the use of neostigmine, and I have identified these cases as being examples of myasthenic myopathy. They may not in fact be examples of true muscular dystrophy, and in any event they are extremely rare.

The latest additions to the list of remedies are the anabolic steroids such as norethandrolone (Nilevar) and methandienone (Dianabol) and similar drugs. These have been shown to prolong the lives of dystrophic mice, but in a recent controlled trial which Dr. Barwick and I have carried out in Newcastle upon Tyne these drugs have been shown to be in no way superior to control tablets when used to treat 30 cases of progressive muscular dystrophy—10 of the Duchenne type, 10 of the limb-girdle type, and 10 facio-scapulo-humeral—over a six-month period.

The complete absence of any effective drug therapy does not, of course, mean that management is not important. It is well known that the symptoms of muscular dystrophy in a young boy may first come to light after a febrile illness, or that weakness in an established case may be greatly and permanently increased after a prolonged period of bed-rest for some other illness. It is therefore vital, particularly in cases of the Duchenne type, that these children should be kept active and be encouraged to walk and to use their limbs as much as possible. This may even mean getting them out of bed after an illness very much earlier than would normally have been appropriate. It is also clear that immobilization of the limbs is contraindicated, as this, too, may produce marked deterioration; and for this reason, if for no other, surgical operations to lengthen tendons and similar procedures are completely out of the question. Care must also be taken to watch for the development of contractures at the elbows, at the knees, and at the ankles, where these are prone to occur. For instance, biceps brachii and hamstring contractures are common in children who spend a good deal of their time in wheelchairs, while contracture of the tendo Achillis may result in an equinovarus position of the foot. I always advise parents to carry out passive stretching of tendons in which contractures are beginning, two or three times daily, though I

am very dubious whether this measure is at all successful in halting the development of these complications. It is also of great importance to bear in mind the fact that skeletal distortion and atrophy, which may be very severe, are a common sequel of the muscular disease (Walton and Warrick, 1954), and some of the long bones, such as the humerus and even the femur, may become pencil-thin and somewhat decalcified as a result of the muscular weakness; and these bones are liable to be fractured on minimal trauma, so that very careful handling is vital.

Lastly, so far as "pure" muscular dystrophy is concerned, the importance of genetic counselling must be stressed. When a mother has had one child with the Duchenne-type dystrophy it is never possible to be sure whether she is in fact a carrier unless the disease appeared in her brothers, when it can be taken as certain that she carries the gene. If this is not the case, it is possible that the disease in her child arose as a result of mutation and that it may not recur in subsequent sons; but, on the whole, I think it is reasonable to accept, under these circumstances, that there is a 50% chance of the disease developing in any subsequent sons. We do not know for certain whether mutation usually occurs in single germ cells or in a segment of ovary. Similarly, the sisters of boys with Duchenne-type dystrophy generally have a 50% chance of being carriers themselves and of passing on the disease to half their sons. In the limb-girdle variety of the disease it is very unlikely indeed that the affected individual will pass on the disease to his children provided the pattern of inheritance is typical of an autosomal recessive mechanism, as he would only do so if by a most remarkable coincidence he were to marry a heterozygous carrier of the gene. Intermarriage does, of course, greatly increase the incidence of this variety of the disease, and hence consanguinity is to be discouraged in families in which this disease has previously been present. Fortunately, the facio-scapulo-humeral type is the most benign, but in this condition it is more than likely that the affected individual will pass on the condition to half his or her children of either sex. Information of this nature is, of course, of great value when talking to patients or their relatives, who are naturally concerned about the future.

A very important advance would be made if it were possible to identify the female carriers of the sex-linked recessive gene responsible for the Duchenne-type dystrophy. We have investigated this possibility very thoroughly using the urinary creatine and creatinine output and the level of the serum aldolase as a guide, but unfortunately these investigations have been entirely negative (Leyburn, Thomson, and Walton, 1961). A recent report by van den Bosch (1961) suggests that an electromyographic technique may possibly give the answer, but this is being studied at the moment, and we are repeating the investigation in Newcastle upon Tyne to see whether we can confirm van den Bosch's views.

MYOTONIA

I will now turn to a brief consideration of cases of muscle disease in which myotonia is a prominent symptom or physical sign. Myotonia is the phenomenon

in which there is an after-contraction or failure of relaxation on the part of voluntary muscle when voluntary innervation ceases. This can be clearly demonstrated in the patient who grips an object and is then unable to let go, and percussion of a muscle gives a dimple which may persist for several seconds before complete relaxation occurs. Myotonia is seen in three principal conditions—myotonia congenita, dystrophia myotonica, and paramyotonia. In myotonia congenita (Thomsen's disease) it is present from birth, persists throughout life, and involves the entire skeletal musculature; while in dystrophia myotonica the myotonia affects particularly the peripheral muscles of the limbs, it may not appear until the disease begins in adult life, and is associated with frontal baldness (in the male), cataract, gonadal atrophy, facial myopathy, weakness of the sternomastoids, a peripheral myopathy in the limbs, and often with an increased thickness of the vault of the skull and an unusually small sella turcica. Not uncommonly there is associated hyperostosis frontalis interna. Paramyotonia congenita, by contrast, as first described by Eulenberg (1886), is similar to myotonia congenita except that the myotonia occurs only on exposure to cold and is often followed by attacks of generalized muscular weakness which closely resemble the episodes seen in patients with familial periodic paralysis.

The interrelationship of the various conditions within this group is a matter of considerable dispute. Many workers consider that they are entirely different, while others feel that they are closely related or that they may in fact be variants of a single basic disease process. There can be no doubt that the natural history of the average case of myotonia congenita contrasts sharply with the natural history of the illness as seen in the typical case of dystrophia myotonica. The first is a benign affliction producing comparatively little disability in the majority of cases, while the second is a progressive, crippling disease. On the other hand, everyone who has studied cases of this type must be aware that a great many intermediate cases occur which seem to represent a transition between the two diseases. Nevertheless, it is still impossible to give a definite answer on the question of classification. Recent work has, however, clearly shown that in paramyotonia the attacks of muscular weakness are very closely related to the episodes of paralysis which occur in patients with familial periodic paralysis, but in fact in most families with paramyotonia the attacks have been associated with a rise in serum potassium rather than with a fall, so that the condition is more closely related to the so-called adynamia episodica hereditaria of Gamstorp (1956). Many observers, including myself, now feel that in all probability paramyotonia, which is in fact a rare condition, is due to a chance association between myotonia congenita on the one hand and periodic paralysis or a related condition on the other, in the same family.

In passing, it is important to mention briefly the question of pseudomyotonia. There is no doubt that a symptomatic phenomenon closely resembling myotonia may develop in patients with progressive muscular atrophy, polyneuritis, and in some with a variety of other neurological diseases. Equally, and probably much

more, common is the phenomenon of slow muscular contraction and of relaxation which is seen in patients with hypothyroidism, and we have recently studied a number of cases of this type. The phenomenon is clinically and electromyographically different from myotonia, but yet there is a certain superficial clinical resemblance, so that myxoedema of the muscles should always be borne in mind in patients complaining of pain and aching and stiffness and cramp following exertion (Wilson and Walton, 1959).

Treatment

A number of effective remedies are now available for the control of myotonia. In patients with myotonia congenita, in whom this is the sole cause of disability, such treatment can be very effective indeed. It has, of course, been known for years that quinine will relieve this symptom, though it may have to be given in rather high dosage with consequent toxic side-effects. More recently, however, it has become apparent that procainamide (Geschwind and Simpson, 1955) and cortisone or prednisone (Liversedge and Newman, 1956) are both very effective in the relief of myotonia. A controlled trial carried out by Leyburn and myself (1959) showed that procainamide was probably the better remedy if given in a dosage of 250 mg. four times daily, increasing up to a maximum dose of 750–1,000 mg. four times a day, though very few patients can tolerate the maximum dose. There are some patients with dystrophia myotonica in whom myotonia is a prominent symptom, and these too can be greatly helped by these remedies. In our hands ion-exchange resins (Leyburn and Walton, 1960), which some have found to be successful in controlling myotonia by the reduction of the serum potassium, have been disappointing, and I am sure that procainamide is at present the drug of choice, though for the occasional resistant cases prednisone in a dose of up to 20 mg. daily should be tried. So far as the myopathic change which occurs in dystrophia myotonica is concerned, there is no effective treatment for this condition as in any variety of progressive muscular dystrophy, but the same principles mentioned previously in connexion with muscular dystrophy apply, and it is important that the patient should remain active for as long as possible.

POLYMYOSITIS

This is a syndrome of considerable interest. I appreciate that the existence of this disease has been challenged, and there are many like myself who are aware that within the diagnostic category of polymyositis we may be including two or three, if not more, totally different diseases. Nevertheless, I am sure that all will agree that we are coming to recognize more and more a category of illness for which no other diagnostic label is possible even though we still know comparatively little about its aetiology and pathogenesis. Without doubt the great majority of cases falling into this category are suffering from a disease which is closely related to the other

disorders of the so-called "connective-tissue" group, but whether this is true of all cases remains uncertain, and there are a great many other problems concerning the nosology of this condition which remain obscure (Walton and Adams, 1958).

Leaving aside arguments concerning aetiology, classification, and pathogenesis, it will readily be agreed that polymyositis is broadly a condition which affects particularly the proximal muscles of the limbs; it may begin at any age, though this largely depends on the clinical type. In some cases the clinical features indicate that the disease process is, for practical purposes, located entirely within the skeletal muscles, and there are no skin changes and no other manifestations of "collagen" disease. The acute variety of polymyositis can occur at any age, whereas the subacute type is most common in early adult or middle life. Chronic, slowly progressive cases of this nature particularly tend to occur in middle and late life, and this is undoubtedly the syndrome which has been referred to in the past as menopausal muscular dystrophy (Shy and McEachern, 1951).

A second clinical category of cases can be distinguished in which the muscular symptoms and signs are again predominant, but in which there are minimal skin changes, often in the face and fingers, resembling acrosclerosis. This variety of the illness is common in childhood or adolescence, but there are a number of other very similar cases in which the related abnormalities are not in the skin, but in the joints, and resemble minimal rheumatoid arthritis. In yet a third category of cases the dermatological manifestations, which may be very variable and may sometimes resemble scleroderma or acrosclerosis or even exfoliative dermatitis or lupus erythematosus, are predominant and the muscular weakness is, in a sense, a secondary manifestation, or else the patient may have florid changes of rheumatoid arthritis or disseminated lupus erythematosus with which a minimal or unobtrusive polymyositis is associated. This latter type of case is generally referred to as dermatomyositis, and it is in this group that there is a very close relationship with malignant disease, not only in the lung but in other systems. Hence in this variety particularly, but also in all cases of polymyositis, a careful search for a malignant neoplasm is an essential part of management, as the muscular disease often precedes any overt clinical manifestations of the tumour by several months and even occasionally years.

Treatment

The treatment of polymyositis is an extremely difficult and complicated problem. I only wish I could say that the height of the erythrocyte sedimentation rate, findings on muscle biopsy or on electromyography, the electrophoretic pattern of the serum proteins, or the level of the serum aldolase and transaminase were valuable guides to the expected response to treatment. Unfortunately this is far from being the case. The sheet-anchors of treatment are prednisone and related drugs. It is true that some cases of myopathy resulting from prednisone therapy and from therapy with cortisone and other derivatives have been described, and it is parti-

cularly evident that triamcinolone and dexamethasone show this tendency to give rise to muscle necrosis in very marked degree. Triamcinolone, in fact, appears to be a direct muscle poison and should no longer be used as a therapeutic agent. Despite this difficulty, there is no doubt that prednisone therapy in polymyositis is the only really effective form of treatment, and should be tried in every case in which the diagnosis is established by a combination of clinical and ancillary findings, even in the cases where cellular infiltration in the muscle biopsy specimen is slight or minimal and where the E.S.R. is normal. In my experience the most useful guides to the diagnosis of polymyositis are a combination of clinical findings and electromyography. The other tests, and muscle biopsy itself, are only sometimes helpful, and if these investigations are negative they do not by any means exclude the diagnosis.

I always begin with prednisone in high dosage (60 mg. daily) and continue with this dose for several days, ignoring the side-effects, until some clinical response appears. It is almost invariably necessary to give, in addition, antibiotics such as penicillin or one of the tetracyclines, particularly in acute dermatomyositis, because of the ever-present danger of respiratory infection. No such precaution is, however, necessary in the average case of mild or subacute polymyositis, and everything depends on the general condition of the patient. Once clinical improvement has begun it is then possible to reduce the dose gradually, first to 50 mg., then to 40 mg., and then perhaps to 30 mg. daily, and this level should be continued for several weeks until it is quite clear that the patient's improvement is continuing. The guiding principle must be that the patient should receive the minimum dosage necessary to control his symptoms and physical signs, and any sign of deterioration, however slight, should be an indication to increase the dose again to the next highest level.

Patients with acute polymyositis and subacute polymyositis and those in whom skin changes are relatively unobtrusive respond best to this treatment. The response on the whole is much less good in florid cases of dermatomyositis, and there are indeed a few patients with this condition, and even a few with uncomplicated polymyositis, who for some obscure reason show no response at all, and either deteriorate rapidly with a fatal outcome or else go on deteriorating slowly without significant change in the natural history of the disease. The latter course of events is seen particularly in a small proportion of cases of chronic polymyositis arising in late life. In my experience, however, the response is better the earlier in the course of the illness the treatment is started, and patients in whom treatment is begun within a month of the onset usually do well. We are at present in process of analysing the results of treatment in a series of 60 patients with polymyositis treated in the Newcastle upon Tyne area in the last five years, and it appears that a reasonable response to steroid therapy has been achieved in almost 80% of cases.

One can, however, distinguish a very definite category of cases in which

there is initially a rather poor response to treatment, and in which after a few months of slight or moderate improvement there is a gradual decline in the patient's health despite continuation of steroid therapy. This pattern is almost diagnostic of associated malignant disease, even though the presence of a tumour may not be detected until after death. It is also apparent that, whereas some patients make a complete recovery and their treatment can be stopped after twelve to eighteen months or so, there are others in whom improvement reaches a certain point and then seems to stop. Long-continued steroid treatment is still required in order to prevent relapse in such cases, and it seems that, whatever one does, complete recovery is impossible to achieve. However, I am now following up a series of patients who have been under treatment for periods varying from one to three years but in whom the drugs have eventually been discontinued without relapse of their disease.

In this connexion a word should be said about other methods of treatment which are occasionally necessary. In a small proportion of the very acute cases in which there is severe dysphagia with a tendency to choke it is necessary to do tracheotomy, which can be a life-saving measure and certainly renders nursing much easier. In a very small number of cases assisted respiration is needed. In view of the associated weakness of the muscles of deglutition, intermittent positive-pressure respiration is much more satisfactory than nursing in a tank respirator or in a cuirass. I have now seen two patients with polymyositis who have required long-term nursing on intermittent positive-pressure respiration but who have recovered, though in another two similar cases the illness ended fatally after a long and difficult illness. There is also evidence to suggest that to give anabolic steroids such as norethandrolone or methandienone or one of the several similar preparations is of some value in assisting recovery once a clinical response to prednisone has begun, though it is extremely difficult to obtain satisfactory scientific evidence to support this point. Certainly steroid therapy has transformed the natural history of this disease and far more patients now recover than in the past.

MYASTHENIA GRAVIS

I do not propose to consider in any detail the diagnosis of this condition, except to say that there appear to be two principal categories of myasthenia which differ considerably from the point of view of prognosis. The first is the ocular variety, in which the condition appears to remain confined to the ocular muscles for many months or years, if not permanently, and in which the prognosis is excellent so far as life is concerned, though eventually a considerable degree of permanent weakness and degeneration in certain of the external ocular muscles takes place. There is a much larger group of cases in which the muscles of chewing and swallowing and those of the limbs are involved. No ocular case is ever fatal, but there is a considerable risk of fatality in a proportion of cases of the generalized

variety. It is clearly apparent that a myasthenic syndrome indistinguishable from the so-called idiopathic disease can occur in patients with malignant disease, particularly in the lung. Furthermore, a particularly florid variety of myasthenia gravis is sometimes seen in patients who have a thymoma, and even if the thymic tumour is not itself malignant the myasthenia may be poorly responsive to treatment in such cases.

It is important here to mention some of the recent information which has been collected regarding the natural history of myasthenia gravis. It has, for instance, become clear that the maximum activity of the disease is within the first five years after the onset and that after that period it tends to burn itself out. In other words, if the patient survives five years the outlook is, on the whole, good, and most of the deaths occur within the first two or three years. A substantial proportion of cases show remissions and relapses, but these, too, become progressively less frequent after the first five years of the disease. Simpson (1960) has recently pointed out from an age distribution curve and from a curve of the activity of the disease in a series of cases that the pattern of this illness resembles that of polymyositis. He has also remarked upon the frequency with which allergic or hypersensitivity reactions are associated with myasthenia, and on the frequency with which there appear to be emotional precipitants of the illness. He suggested that the condition might be due to an autoimmune antigen–antibody reaction involving end-plate protein, and it is of some interest that a preliminary report from the United States suggests that such antibodies may indeed be present. This comment would be incomplete without brief reference to the recent studies on nerve-endings in skeletal muscle in patients with myasthenia gravis. The valuable work of Dr. Woolf and his co-workers in Birmingham (Bickerstaff and Woolf, 1960) and of MacDermot (1960) in London has shown that there are certain consistent changes in the terminal intramuscular nerve-endings in patients with myasthenia gravis. This has led these workers to suggest that the disease may be due to a physical abnormality of the terminal nerve-endings. I myself am inclined to the view that Simpson's explanation is the more likely and that the changes in the terminal intramuscular nerves are probably secondary to the disease of the muscle cell and of its fibre membrane, but it is too early to express a definite opinion on this point and the disease remains one of considerable interest.

Treatment

So far as drug treatment is concerned, neostigmine and pyridostigmine (Mestinon) are still the most effective preparations. It is my usual practice to begin gradually with one tablet (15 mg.) of neostigmine four times daily together with 1/100 gr. of atropine twice daily. I give atropine as an invariable rule to overcome the muscarinic side-effects of the neostigmine, as I find that many patients with myasthenia develop abdominal pain and sometimes diarrhoea or nausea if they are not given atropine. I then increase the dose steadily, depending on the

patient's requirements and clinical response. This is one disease more than any other in which the patient is far better able to judge the dose he or she requires than is the doctor. Usually the tablets must be given at least three-hourly throughout the day to be really effective, and often patients can take as many as four, five, six, or even more tablets every three hours throughout the day to achieve maximum response. Pyridostigmine can sometimes be added, and is particularly useful given in 60-mg. tablets last thing at night, as it has a long-acting effect and usually helps the patient to wake up much less weak the next morning. Ephedrine, 0·5 mg. three times a day, is sometimes a useful adjuvant. The newer drugs such as Mytelase do not seem to have much advantage over the traditional remedies. Tensilon (edrophonium chloride) is not, of course, of any value in treatment, as its effect is so transient. It is this extremely transient effect which makes it useful as a diagnostic aid. It is also particularly useful in deciding whether, when a patient with myasthenia appears to be deteriorating despite neostigmine treatment, this is in fact due to a deterioration in the myasthenia or because he is having too much neostigmine which is producing a depolarization block in the muscle-fibre membrane. In such a case an intravenous injection of 10 mg. of Tensilon can be given. If this improves the patient's weakness it suggests that the dosage of neostigmine is too low, while if it makes him weaker it suggests that it is probably too high. To assess the effects of this test may be difficult, but with experience it can be extremely useful.

Here it is important to say something about thymectomy. Arguments have raged for years as to the value of this form of treatment. Some authorities have said that it is the only really effective treatment and that it is virtually indicated in every case, while others have refused to have their patients operated upon. I am sure neither of the extreme views is true, and Simpson's results published in 1958 seem clearly to indicate that thymectomy is very helpful if done in severe cases, particularly in young females, at an early stage of the disease. In other words, we must be extremely selective. Even so, it would be unwise and unsafe to do a thymectomy on a patient with a thymoma unless preliminary radiotherapy had been given.

METABOLIC MYOPATHIES

Finally I would like to consider some of the interesting metabolic myopathies, a group of disorders which is being added to almost every day. It has, for instance, become abundantly clear in recent years that many of the common endocrine diseases may produce or be associated with changes in the voluntary muscles. Acute and subacute thyrotoxic myopathy responding to treatment of the thyrotoxicosis by surgery or by drugs has been known for many years, but it is only comparatively recently that myopathic conditions have been described in patients suffering from Addison's disease, hypopituitarism, and Cushing's syndrome. The descriptions of these conditions are quite convincing, but they need not detain us long, since, although they are of considerable interest from the diagnostic and

aetiological standpoints, each of these conditions responds well to treatment of the primary endocrine abnormality.

Familial Periodic Paralysis

However, I would like to give some consideration to familial periodic paralysis and the related clinical entities which have recently been described. The classic variety of familial periodic paralysis is the hypokalaemic form, in which the attacks are associated with a fall in serum potassium level. Typically the attacks occur on waking in the morning, and may be precipitated by exertion or by a heavy carbohydrate meal followed by a period of rest. The attacks vary considerably in that they may produce no more than a generalized weakness of limb muscles, particularly of the proximal groups, which may sometimes be mild and on other occasions so severe that the patient can barely move a muscle. Muscles of respiration, deglutition, and speech are not as a rule affected. Occasionally the weakness may be asymmetrical, involving one limb more than another, and the pattern of muscular involvement may be consistent from attack to attack. The episodes can also be provoked by the production of an alkalosis or by giving injections of insulin and glucose to metabolize liver glycogen. It has long been known that in most cases the attacks can be terminated by the oral administration of potassium, though long-continued treatment with potassium by mouth has not usually been successful in preventing attacks. Recently Gamstorp (1956) described a condition which is clinically almost identical but which she entitled adynamia episodica hereditaria. In this condition similar attacks occur, but are associated with a rise rather than a fall in serum potassium level. It has been known also for a considerable time that some attacks occur when the serum potassium is within the normal range. A family with this variety of periodic paralysis has recently been studied in Newcastle by my colleagues Poskanzer and Kerr (1961), who have referred to the condition as the sodium-responsive normokalaemic variety of familial periodic paralysis, and they identify this as a third probable variety. Conn and his co-workers (1957) have suggested that in the hypokalaemic variety an intermittent over-production of aldosterone from the adrenal cortex is responsible for the attacks, but recent investigation has shown that this is almost certainly not the explanation. Shy and his co-workers (1961) in a very extensive investigation have shown that in the attacks of paralysis the muscle cells may contain numerous vacuoles and that between them are areas of dilated endoplasmic reticulum which are swollen with glycogen. They have also demonstrated that even at the height of paralysis a microelectrode inserted into the muscle cell gives a normal potential, indicating that there is no gross imbalance of ions on either side of the fibre membrane. They produce cogent reasons for suggesting that the attacks are accompanied by a marked shift of water into the muscle cell rather than by a primary shift of sodium or potassium. Their evidence seems to indicate that the

disease may in fact be due to a curious defect of glycogen anabolism, but this explanation too remains rather speculative, and one cannot as yet be certain why the varieties of periodic paralysis show such striking biochemical differences.

However, despite the variable clinical picture and the variable severity of the illness in different cases, the outlook for most patients with periodic paralysis of whatever type is, on the whole, good. For instance, one of my patients who has had the condition since early childhood is now a policeman, still working on the beat in his middle fifties; another is a trawler fisherman; while yet another, who is in his thirties, is a bus conductor. I have yet to see a patient who is seriously disabled by familial periodic paralysis except in the attacks, and we are beginning to achieve some success in the control of the attacks themselves. In a small proportion of cases it must, however, be accepted that after repeated attacks of paralysis, particularly if these are severe, there is some eventual muscular weakness and wasting which is irreversible by any form of treatment, but fortunately this is usually comparatively slight.

Treatment

Treatment must depend upon the type of the illness. In the classic hypokalaemic variety potassium given during the attacks and prophylactically is helpful, but even more effective in some cases is sodium restriction. Adynamia episodica hereditaria, the variety in which the serum potassium level rises during the attacks, is much the most easy to control. Long-term treatment with acetazolamide (Diamox) or chlorothiazide has, in my experience, been most effective in controlling the attacks. The fisherman already mentioned, who falls into this category, was completely free from attacks while on chlorothiazide treatment, and this continued until his general practitioner substituted chlorothiazide-K tablets; immediately the potassium supplement was added the attacks began again. The only other important precipitant is that on occasion on returning from a voyage to sea he will drink far more beer than is good for him and may then become paralysed in the physical as well as in the semi-metaphysical sense. The reason for this course of events is that beer contains a considerable quantity of potassium.

Finally, recent work, not yet fully confirmed, suggests that the aldosterone inhibitors such as spironolactone and its analogues may prevent the attacks, particularly in patients with the sodium-responsive normokalaemic variety of the illness (Poskanzer and Kerr, 1961). Investigations of the effects of these remedies are, however, only preliminary, and there is every likelihood that more advances will be made within the next few years.

McArdle's Syndrome

I would like lastly to mention among the group of metabolic myopathies the rare but interesting condition now widely called McArdle's syndrome. McArdle in

1951 first described a curious variety of muscle disease which gave rise to widespread muscular pain and cramps following exertion. He demonstrated that this disorder was due to a defect in muscle glycogen breakdown. More recently Schmid and Mahler (1959) and Pearson (1961) have clearly demonstrated that this condition is due to absence of muscle phosphorylase and that it is therefore an unusual and rare variety of glycogen-storage disease of muscle. This diagnosis should be considered in all cases in which severe muscular pain and cramp follow exertion, particularly if these symptoms have been present since birth. Therapeutically the outlook is not yet very hopeful, though recent work suggests that intramuscular injections of large quantities of glucagon may be helpful. It has also become apparent that the condition may occasionally affect more than one member of a family and that the episodes of severe muscular pain following exertion may be associated with myoglobinuria. It may therefore be that some patients described in the past as examples of paroxysmal myoglobinuria may in fact have been suffering from this congenital phosphorylase deficiency.

CONCLUSIONS AND SUMMARY

There are still a great many unanswered questions in the field of muscular disease. Those who take a particular interest in this group of diseases can never fail to be dismayed by the progressive downhill course of patients with muscular dystrophy and by the tragic effect this disease has upon the affected child and his family. It is to be hoped that the research at present being carried out in many parts of the world will eventually lead to the discovery of some effective treatment. In the case of polymyositis, too, we cannot yet be complacent. Much more information is needed about the nosology and pathogenesis of this syndrome, and, although steroid therapy has transformed the prognosis in many cases, there are others which seem totally or partially unresponsive. Recent suggestions that myasthenia gravis may be due to an autoimmune antigen–antibody reaction indicate that the relationship of this condition to polymyositis and to the collagen diseases must be carefully scrutinized; while in the field of metabolic myopathy the many advances in knowledge now being made raise problems which are likely to occupy us, and our colleagues in full-time research, for many years to come. Truly muscular disease is now more than ever a fruitful field of study.

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[*Concluded at foot of p. 134*

THE EIGHTEENTH ANNUAL MEETING

THE eighteenth Annual Meeting of the British Association of Physical Medicine was held on April 21 and 22, 1961, at the Westminster Hospital, London, and the Royal National Orthopaedic Hospital, Stanmore, with the President, Dr. Hugh Burt, in the chair.

SCIENTIFIC MEETING

On the morning of Friday, April 21, the following papers were presented:

"Viscero-somatic Reflexes", by Dr. A. MCPHERSON
"Staphylococcal Osteomyelitis of the Spine", by Mr. C. W. MANNING
"Chondrolysis", by Dr. CHARLES LACK
"Study of Bone Growth by Tetracycline Markers", by Dr. W. R. LEE

In the afternoon there was a symposium on "Disabilities of the Hand" comprising the following papers:

"The Rheumatoid Hand", by Dr. D. A. BREWERTON
"Peripheral Nerve Injuries", by Mr. H. J. SEDDON
"Rehabilitation of the Hand", by Wing-Cdr. C. B. WYNN PARRY
"Reconstructive Surgery", by Mr. D. M. BROOKS.

On Saturday, April 22, three short papers were presented:

"Patient, Physician, and Department", by Dr. F. BACH
"Steroid Myopathy", by Dr. D. N. GOLDING, Dr. G. W. PEARCE, and Dr. M. THOMPSON
"Newer Steroids for Local Injection", by Dr. G. HOLDEN and Dr. P. HUME KENDALL

followed by a film entitled "Hydrotherapy Unit at St. Benedict's", by Dr. N. S. CRAIG.

ANNUAL DINNER

The Annual Dinner of the Association was held at Apothecaries' Hall on April 21. In proposing the health of the Association, Mr. H. J. SEDDON paid tribute to the astounding changes which had taken place in the eighteen years of the Association's existence; in particular the insistence on higher medical degrees, the increasing influence in the clinical field, and the discouragement of eccentricities in therapeutics. He drew attention to the disquieting situation in the North of England, where there was a great shortage of specialists in physical medicine; the appointment of a physician in physical medicine to the Royal National Orthopaedic Hospital had proved a great success, and he could only believe that antagonism to such appointments was due to a mixture of ignorance and misunderstanding.

In reply, the PRESIDENT thanked Mr. Seddon for bridging the gap between orthopaedics and physical medicine, and for his help in allowing the Association to meet in the Mecca of orthopaedics.

The health of the guests was proposed by Dr. R. M. MASON, and Mr. A. C. H. BELL, President of the Royal College of Obstetricians and Gynaecologists, replied.

ANNUAL GENERAL MEETING

The Annual General Meeting was held at Westminster Hospital on Saturday, April 22. The annual report of the Council and reports from the Honorary Treasurer and Honorary Editor were received.

The following officers were elected for 1961–2:

Vice-President:	Dr. W. S. Tegner
Honorary Treasurer:	Dr. J. Shulman
Honorary Secretary:	Wing-Cdr. C. B. Wynn Parry
Honorary Editor:	Dr. A. C. Boyle
New Members of Council:	Dr. Logie Bain
	Dr. D. M. L. Doran
	Dr. Joyce Lomas
	Dr. R. I. Meanock
	Dr. A. T. Richardson.

An amendment to the rules of the Association, creating a new class of Associate Membership, was approved. In future, in addition to Honorary Members and Honorary Life Members, there will be the following classes of Membership: (*a*) Full Members; (*b*) Associate Members; and (*c*) Overseas Members.

All present Full Members of the Association will be entitled to retain Full Membership if they so wish. Future admission to the Association will be through Associate Membership, and Full Membership will be restricted to medical practitioners resident in the United Kingdom or Eire, and of consultant or S.H.M.O. status within the National Health Service or its equivalent; Full Members must also be predominantly engaged in the practice of physical medicine.

NORTH AND MIDLANDS PHYSICAL MEDICINE CLUB

THE seventh Annual Meeting was held at the Army Medical Rehabilitation Unit, Saighton Camp, Chester, on March 25, 1961, with Lieut.-Col. J. B. M. Milne in the chair (Secretary: Capt. D. S. Smith).

In the morning, after the business meeting, Lieut.-Col. J. M. Matheson, Surgeon to the Cambridge Military Hospital, gave a talk on "Some Aspects of Surgery in the Peacetime Army". This was followed by a short introduction to the Unit by Lieut.-Col. Milne, and members then adjourned for sherry and lunch.

After lunch members were taken on a conducted tour of the Unit, seeing a shortened version of a normal day's programme. There was then a short intermission to watch the Grand National on television. This was followed by a lecture by Lieut.-Col. R. Fuller on "The Army Treatment Regime of Reiter's Syndrome". Capt. P. Pearson then gave a short analysis of some of last year's results. A lively discussion ensued. Finally, in the afternoon, a number of unusual cases were demonstrated by Capt. D. S. Smith, which provoked considerable discussion.

The meeting was honoured by a number of distinguished guests, including Dr. Hugh Burt, President of the British Association of Physical Medicine, in his capacity as Civilian Consultant to the Army.

REVIEWS OF BOOKS

MAN'S POSTURE: ELECTROMYOGRAPHIC STUDIES. By J. Joseph. *Pp. 77. 44s. Oxford: Blackwell. 1960.*

In just under 80 pages the author describes the method he uses for the detection of electrical activity in muscles as well as results and conclusions. His studies are restricted to muscle groups responsible for the maintenance of the erect posture in man.

The use of a very high gain and low noise level amplifier has enabled him to carry out his studies on superficial muscle by means of surface electrodes. His technique has made him confident that electrical silence from his equipment could be interpreted in terms of absence of all muscular activity. While accepting this for immediately subcutaneous muscles, the reviewer questions the wisdom of drawing similar conclusions where the iliopsoas is concerned. This muscle, unlike the sartorius and adductor longus, is not truly subcutaneous inasmuch as it is separated from the skin by the content of the femoral triangle. It is a pity that he did not check his own results with needle electrodes in this particular case instead of gratuitously and unconvincingly casting doubt on Dr. Basmajian's findings.

Dr. Joseph devotes an interesting page in the first chapter of his monograph to the uniqueness of man's posture, but the results rightly show that the variations are numerous, and one is driven to the conclusion that in this respect all men may well be unique but that some are more unique than others.

This book is easy to read and well illustrated, and points the way to the clinical investigation of muscle imbalance, whether due to faulty skeletal architecture or posture.

P. BAUWENS

CIRCULATORY ULCERS. A PHYSICAL APPROACH. By Hilton G. Tranchell and Charles R. Bannister. *Pp. 91. 12s. 6d. Bristol: Wright. 1960.*

The preface tells us that treatment of tropical ulcers in a prisoner-of-war camp began the experience of one of the authors. It is clear from the text that they have a great deal of experience and knowledge of their subject. The main object of the book is to instruct students of physiotherapy in the subject of leg ulcers and their treatment by physical methods. Unfortunately the clarity of presentation, logical order, and emphasis on essential basic facts necessary for the teaching of students are missing. Medical terminology is used in a lax manner and the general effect is untidy. Much good material is there, but it is put together in haphazard fashion. For example, the vital question of elastic support for the limb is correctly stated by the authors to be "possibly the most important single factor in the treatment of these cases". This is tucked away in a chapter on "Aims and Techniques of Treatment" behind the camouflage of a main subheading "To Relieve Pain", and even then it appears as the fifth subdivision of the second subsection of that heading, after such relatively unimportant treatment as anodal galvanism.

There are certain omissions, notably in the section on the underlying pathology of gravitational ulcers. No mention is made of incompetent perforating veins following deep-vein thrombosis as described by Cockett. This is important, as it supplies the pathological concept which gives logic to the work of Bisgaard and the good results obtained by adequate support and physical treatment.

Qualified physiotherapists who have to treat leg ulcers will find interest and instruction in this little book if they are prepared to look for it. My advice to students is to keep away from it, which is a pity, as it could have been so good.

I. H. M. CURWEN

LES MANIPULATIONS VERTÉBRALES. By Robert Maigne. *Pp. 246. NF. 28. Paris: Expansion Scientifique Française. 1960.*

This is a carefully written book divided into four sections. In the first manipulation is defined and described, theories involved are explained, and practical application of treatment and possible results given. The second part is devoted to a detailed and clearly illustrated description of technique of manipulation of the spinal, costal, and some limb joints in the osteopathic manner. The third part gives indications for manipulative treatment in various clinical conditions. In the fourth part R. Lescure discusses the possible visceral effects of manipulation, and a method of following up manipulation by remedial exercises based on parallel concepts is described by R. Waghemacker.

The merit of the book lies in the detailed description of manipulative technique and the clear diagrams and photographs which illustrate it. Maigne's discussion of the local pathology of lesions in the intervertebral joints and neighbouring structures is somewhat prolix. It is certainly ingenious, but when carefully analysed does not advance our knowledge beyond already widely held concepts; as the author himself admits, much is still based on hypothesis. This means that treatment, although effective, must still bear the label empirical. Lescure's discussion is a compromise between accepted medical views and the osteopathic theory.

In general, the approach is more acceptable to the ordinary medical reader than other works on osteopathy, apart from Stoddard's recent book. The fact that these two books have appeared is an indication of the increased interest in and use of manipulation among doctors and qualified physiotherapists. They are to be welcomed as signs of the adoption of a useful method of treatment which for too long has been the almost exclusive province of the unqualified manipulator.

I. H. M. CURWEN

"The Prognosis and Management of Some Muscular Diseases", by JOHN N. WALTON
(continued from p. 130)

KILOH, L. G., and NEVIN, S. (1951) *Brain*, **74**, 115.
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ABSTRACTS OF THE LITERATURE

Effects of Short Bouts of Isometric and Isotonic Contractions on Muscular Strength and Endurance. C. E. WALTERS, C. L. STEWART, and J. F. LECLAIRE. *Amer. J. phys. Med.*, 1960, **39**, 131.

In a study of muscular strength and endurance 15 subjects were divided into three groups and trained in elbow flexion. One group held its full isometric tension for 45 seconds, one held two-thirds of its full isometric tension for the same time, and the third group lifted one-third of its one-lift maximum as fast as possible within 45 seconds. All groups were tested for strength and endurance before, and at three and eight weeks after, the study.

All three methods were found to be effective in the development of strength, but the isometric method was superior. All methods resulted in increase in strength in the untrained arm.

C. B. WYNN PARRY

Nutrition and Athletic Performance. J. MAYER and B. BULLER. *Physiol. Rev.*, 1960, **40**, 369.

The authors review the knowledge concerning the optimum diet for athletes, stressing the difficulties in clinical research in this field. They conclude that athletes require no less than three meals a day. If sport is protracted and exhausting, they suggest that five lighter meals would be better than three large meals. Sports involving tests of endurance are better performed with a high-carbohydrate diet. Protein is not needed over and above the normal content of the diet. Claims for vitamin E and wheat-germ oil have not been substantiated.

C. B. WYNN PARRY

Prevalence of Rheumatoid Arthritis. J. S. LAWRENCE. *Ann. rheum. Dis.*, 1961, **20**, 11.

The author has used the data from two surveys, based on a 1 in 30 random sample of persons aged 15 and over, to determine the prevalence of rheumatoid arthritis. The first was carried out in Leigh, Lancashire (sample 75 males and 814 females), and the other in Wensleydale, Yorkshire (sample 485 males and 540 females). Patients were classified according to the criteria of the American Rheumatism Association after clinical, radiological, and serological study.

Definite disease was found in 0·4% males and 1·4% females; probable disease in 1·7% males and 3·8% females. Applying these findings it is estimated that in Great Britain in 1956 approximately 377,000 males and 1,034,000 females had "probable" or "definite" rheumatoid arthritis.

MAURICE F. HART

Arteritis in Rheumatoid Arthritis. F. R. SCHMID, N. S. COOPER, M. ZIFF, and C. MCEWEN. *Amer. J. Med.*, 1961, **30**, 56.

In this paper are described 17 cases of arteritis developing in patients with rheumatoid arthritis; full case histories are given. It is suggested that the finding of episcleritis, peripheral neuritis, and the presence of L.E. factor in the serum indicates necrotizing arteritis. There is no support for the suggestion that cortisone may be the causative factor.

MAURICE F. HART

Transfusion Studies in Rheumatoid Arthritis. J. HARRIS and J. A. VAUGHAN. *Arthr. and Rheum.*, 1961, **4**, 47.

The authors describe a series of transfusion studies made in an attempt to ascertain whether there was a transmissible factor which could induce any stigmata of rheumatism in the recipient. Plasma or plasma and peripheral leucocytes containing a high rheumatoid agglutinating factor was used. The only response noted was a transient rise in E.S.R. and fall in leucocyte count. A two- to three-year follow-up failed to show any evidence of rheumatoid arthritis in the recipient.

M. HOLROYD

Osteoarthritis of the Hip. O. E. AUFRANC. *Arthr. and Rheum.*, 1961, **4**, 94.

The author discusses the surgical management of osteoarthritis of the hip, indicating the reasons for the particular choice of operation in each case, and stressing the importance of after-care. Cases operated on 20 years ago still have good function, and other patients over 80 years of age have benefited greatly by the operation. A number of radiographs are reproduced.

M. HOLROYD

Current Methods of Treatment in Osteoarthritis of the Hip. O. STEINBROCKER. *Arthr. and Rheum.*, 1961, **4**, 89.

The indications for instituting the various methods of treatment, especially medical, in osteoarthritis of the hip are discussed. Pain is usually the outstanding complaint necessita-

ting early surgical intervention in some patients; in others the deterioration is slow and surgery is not required. The elderly may be unfit for operation. Some patients have a marked psychological barrier, refusing surgery.

General and local measures are discussed in detail, but considered as generally only a delaying tactic prior to surgery.

M. HOLROYD

Nine Years of Experience with Intrasynovial Steroid Therapy. J. L. HOLLANDER, R. A. JESSAR, M. A. BOWIE, C. R. STEVENSON, E. M. BROWN, L. UDELL, and J. R. SHANAHAN. *Arch. interamer. Rheum.*, 1960, **3**, 171.

The authors review their experience over nine years with more than 100,000 injections in nearly 4,000 cases. They compare the effects of many of the newer preparations, but believe that none has shown any particular advantage over prednisolone *t*-butyl acetate. They consider that serious complications are extremely rare; infection of the joint occurred in only 14 of their cases. Deterioration of the joint with the production of a painless flail joint occurred in less than 1% of cases.

G. O. STOREY

Non-infectious Arthritis in Small Bones and Joints. Roentgenologic Manifestations. R. F. SCALF and J. T. LING. *A.M.A. Arch. intern. Med.*, 1961, **107**, 23.

The authors record the radiological manifestations and discuss the differential diagnosis of osteoarthritis, rheumatoid arthritis, gout, psoriatic arthritis, and the osseous changes in sarcoidosis.

MAURICE F. HART

Symposium on Disseminated Sclerosis and Allied Conditions. *Proc. roy. Soc. Med.*, 1961, **54**, 1.

This is an absorbing and important report which deserves to be widely read. It presents much new information and throws out many challenges. There are ten contributors, and the aspects covered include genetic, biochemical, epidemiological, aetiological—in particular theories of autoimmunity—and ophthalmic. Among interesting positive statements are that there is suggestive evidence that disseminated sclerosis is a disease of higher latitudes and of temperate and cold regions; that exacerbations are unlikely in the chronic type of case as a result of pregnancy or surgery; that the disease is significantly commoner in social class 1; that steroids may be useful in acute attacks; that there is evidence of the possible presence in the brain of a potentially lytic substance, lysolecithin; and that the prognosis for vision in retrobulbar neuritis is surprisingly good.

C. B. WYNN PARRY

The Developmental Origin of Spondylolisthesis. L. COZEN. *J. Bone Jt Surg.*, 1961, **43A**, 180.

Two cases are described where spondylolisthesis has occurred as a developmental defect and was not present during childhood. The various theories regarding the aetiology of spondylolisthesis, such as birth injury, pathological process in the pars interarticularis, excessive lumbar lordosis, non-union of stress fracture, etc., are discussed.

MAURICE F. HART

Ochronotic Spondylitis: Report of Two Cases. A. NOGUEIRA and I. BONOMO. *Arch. interamer. Rheum.*, 1960, **3**, 229.

This paper reviews the literature of ochronosis and describes two further cases in a brother and sister. Prednisone was tried in both cases, and the results of treatment are described.

G. O. STOREY

Diagnosis and Treatment of Muscle Diseases. R. M. DOWBEN. *A.M.A. Arch. intern. Med.*, 1961, **107**, 430.

The diseases of skeletal muscles are classified and tests used in their diagnosis (electromyography, muscle biopsy, estimation of serum enzymes and urinary excretion of creatine) are discussed. The muscular dystrophies are described and details of the different varieties given. Other conditions considered are dermatomyositis, polymyositis, Boeck's sarcoid, neuromuscular atrophies, and a miscellaneous group.

This is a useful review presenting a comprehensive classification of muscular diseases, with a discussion of their clinical aspects.

MAURICE F. HART

An Adjustable Lower-extremity Brace. T. L. DELORME, L. JOHNSON, P. LUCHINI, W. BORA, and J. MORRISSEY. *J. Bone Jt Surg.*, 1961, **43A**, 205.

The brace here described consists of calf and thigh bands, two adjustable side-bars or uprights, joints at the knee and ankle, and a clamp for fixing it to the shoe heel. Each component is independently adjustable, making the appliance adaptable to right or left and for patients of most builds. There are good illustrations showing the brace in use under various circumstances; these may be found especially useful in evaluating the type of brace needed for a particular patient.

MAURICE F. HART

ANNALS OF PHYSICAL MEDICINE
VOLUME VI. NUMBER 3. AUGUST 1961

Contents

Annual Subscription 40s. net including postage U.S.A. $7.00

Quarterly, 12s. 6d. net U.S.A. $2.20

PRINTED IN GREAT BRITAIN BY HEADLEY BROTHERS LTD
109 KINGSWAY LONDON WC2 AND ASHFORD KENT